Rev Bras Anestesiol. 2017;67(2):153–165

REVISTA BRASILEIRA DE ANESTESIOLOGIA
Publicação Oficial da Sociedade Brasileira de Anestesiologia
www.sba.com.br

SCIENTIFIC ARTICLE

Postoperative surveillance in neurosurgical patients – usefulness of neurological assessment scores and bispectral index

Silvia Herrero[a,*], **Enrique Carrero**[b], **Ricard Valero**[b], **Jose Rios**[c,d], **Neus Fábregas**[b]

[a] *Universidad de Barcelona, Hospital Clínic, Sala de Recuperación Pós-Anestésicos, Villarroel, Barcelona, Spain*
[b] *Universidad de Barcelona, Hospital Clínic, Servicio de Anestesiología, Villarroel, Barcelona, Spain*
[c] *Universitat Autònoma de Barcelona, Laboratório de Bioestatística e Epidemiologia, Barcelona, Spain*
[d] *Hospital Clínic, IDIBAPS, Bioestadística y Plataforma de Gestión de Datos, Barcelona, Spain*

Received 25 July 2015; accepted 22 September 2015
Available online 12 April 2016

KEYWORDS
Bispectral index monitor;
Craniotomy elective;
Neurologic examination;
Neurosurgical procedures;
Postoperative care;
Postoperative complications

Abstract
Background and objectives: We examined the additive effect of the Ramsay scale, Canadian Neurological Scale (CNS), Nursing Delirium Screening Scale (Nu-DESC), and Bispectral Index (BIS) to see whether along with the assessment of pupils and Glasgow Coma Scale (GCS) it improved early detection of postoperative neurological complications.
Methods: We designed a prospective observational study of two elective neurosurgery groups of patients: craniotomies (CG) and non-craniotomies (NCG). We analyze the concordance and the odds ratio (OR) of altered neurological scales and BIS in the Post-Anesthesia Care Unit (PACU) for postoperative neurological complications. We compared the isolated assessment of pupils and GCS (pupils-GCS) with all the neurologic assessment scales and BIS (scales-BIS).
Results: In the CG ($n = 70$), 16 patients (22.9%) had neurological complications in PACU. The scales-BIS registered more alterations than the pupils-GCS (31.4% vs. 20%; $p < 0.001$), were more sensitive (94% vs. 50%) and allowed a more precise estimate for neurological complications in PACU ($p = 0.002$; OR = 7.15, 95% CI = 2.1–24.7 vs. $p = 0.002$; OR = 9.5, 95% CI = 2.3–39.4). In the NCG ($n = 46$), there were no neurological complications in PACU. The scales-BIS showed alterations in 18 cases (39.1%) versus 1 (2.2%) with the pupils-GCS ($p < 0.001$). Altered CNS on PACU admission increased the risk of neurological complications in the ward ($p = 0.048$; OR = 7.28, 95% CI = 1.021–52.006).
Conclusions: Applied together, the assessment of pupils, GCS, Ramsay scale, CNS, Nu-DESC and BIS improved early detection of postoperative neurological complications in PACU after elective craniotomies.

* Corresponding author.
E-mails: sherrern@clinic.ub.es, silviahn1505@gmail.com (S. Herrero).

http://dx.doi.org/10.1016/j.bjane.2015.09.003

PALAVRAS-CHAVE
Monitor BIS;
Craniotomia eletiva;
Exame neurológico;
Procedimentos neurocirúrgicos;
Cuidados no pós-operatório;
Complicações no pós-operatório

Monitoramento de pacientes neurocirúrgicos no pós-operatório — utilidade dos escores de avaliação neurológica e do índice bispectral

Resumo
Justificativa e objetivos: Avaliamos o efeito aditivo da escala de Ramsay, Escala Neurológica Canadense (CNS), Escala da Enfermagem de Triagem de Delírio (Nu-DESC) e Índice Bispectral (BIS) para observar se, juntamente com a avaliação das pupilas e da Escala de Coma de Glasgow (GCS), melhorava a detecção precoce de complicações neurológicas no pós-operatório.
Métodos: Projetamos um estudo observacional, prospectivo, de dois grupos de pacientes submetidos à neurocirurgia eletiva: craniotomia (Grupo C) e não-craniotomia (Grupo NC). Analisamos a concordância e a razão de chance (OR) de alterações nas escalas neurológicas e no BIS na sala de recuperação pós-anestesia (SRPA) para complicações neurológicas no pós-operatório. Comparamos a avaliação isolada das pupilas e da GCS (pupilas-GCS) com todas as escalas de avaliação neurológica e o BIS (escalas-BIS).
Resultados: No Grupo C (n = 70), 16 pacientes (22,9%) apresentaram complicações neurológicas na SRPA. As escalas-BIS registraram mais alterações que as pupilas-GCS (31,4% *vs.* 20%; $p < 0{,}001$), foram mais sensíveis (94% *vs.* 50%) e permitiram uma estimativa mais precisa das complicações neurológicas na SRPA ($p = 0{,}002$; OR = 7,15, IC 95% = 2,1–24.7 *vs.* $p = 0{,}002$; OR = 9,5, IC 95% = 2,3–39,4). No grupo NC (n = 46), não houve complicações neurológicas na SRPA. As escalas-BIS mostraram alterações em 18 casos (39,1%) *versus* um caso (2,2%) com as pupilas-GCS ($p < 0{,}001$). Alteração na CNS na admissão à SRPA aumentou o risco de complicações neurológicas na enfermaria ($p = 0{,}048$; OR = 7,28, IC 95% = 1,021-52,006).
Conclusões: Aplicados em conjunto, a avaliação das pupilas, GCS, escala de Ramsay, CNS, Nu-DESC e BIS melhoraram a detecção precoce de complicações neurológicas no pós-operatório na SRPA após craniotomias eletivas.

Introduction

Neurosurgical patients have a high risk of neurological complications in the immediate postoperative period increasing both morbidity and mortality[1] and requiring specialized postoperative care. The Neurological Intensive Care Evaluation score is a simple assessment developed and validated specifically to assess the postoperative neurologic status of postoperative cardiac patients.[2,3] It is not a complete neurologic assessment evaluation, and would not be enough for patients who have undergone brain surgery. To the best of our knowledge there is not such a neurological score validated for the postoperative neurosurgical population in the Post Anesthesia Care Unit (PACU). In our institution, we typically use the assessment of the pupillary size and reactivity and Glasgow Coma Scale (GCS)[4] evaluating the mobility of all four limbs.

There are several validated clinical neurological assessment scales, as the National Institute of Health Stroke Scale,[5] the Mini-Mental State Examination,[6] and the Diagnostic and Statistical Manual of Mental Disorders.[7] A major drawback of these assessment scales is that they are long and complex, and therefore not easily applicable for the immediate postoperative period.[8] Other neurologic assessment scales, such as the Ramsay scale,[9] the Canadian Neurological Scale (CNS)[10] and the Nursing Delirium Screening Scale (Nu-DESC)[11] (Appendix A) are better suited to the assessment of extubated postoperative neurosurgical patients in the PACU. The main limitations of periodic evaluations with clinical scales include: inter-observer subjectivity and high inter-observer variability,[11] discontinuous records, observer difficulty in differentiating among levels of deep sedation[12] and the overworked nursing care resulting from their systematic application.

The bispectral index (BIS) (BIS™ brain function monitoring system, Covidien, Boulder, USA) is an index derived from the analysis of electroencephalography scaled to correlate with the depth of hypnosis. Today it has become standard monitoring during general anesthesia. BIS has also proven useful in predicting states of excessive sedation.[13] While some studies show a poor correlation between BIS and the clinical sedation scales,[12,14–16] other studies show that BIS correlates with clinical scales if BIS recordings associated with elevated electromyography (EMG) are excluded.[14,17]

Because BIS records and displays continuously, it has the potential advantage of acting as an early warning signal of any of the neurological complications that are associated with a decreased level of consciousness. On the other hand, the clinical neurologic assessment scales are also useful to detect neurological alterations not associated with decreases in level of consciousness (motor or speech impairment, for instance). To date, we have not found any published studies that have compared BIS with other neurological assessment scales in postoperative neurosurgical patients.

In our hospital, the PACU is the main unit for the postoperative care of patients after elective craniotomies. The Surgical Intensive Care Unit (SICU) is reserved for more complicated cases according to the criteria of neuroanesthesia and neurosurgery. The PACU is equipped for a patient's overnight monitoring if necessary and the patient–nursing ratio can vary from 2:1 to 4:1 depending on the patient's clinical status.

The aim of our study was to assess the usefulness of neurological assessment scales and BIS for the early detection of postoperative neurological complications in the neurosurgical patient. Our hypothesis was that the additive effect of the Ramsay scale, the CNS, the Nu-DESC and BIS to the usual assessment of pupils and GCS would improve early detection of postoperative neurological complications.

Methods

This was an observational prospective study for 6 months (October 2011 to April 2012). The study was approved by the Ethics and Research Committee at our Institution (Number 2011/6854, dated 22-9-2011, Chairman: Gomis R). We asked permission and obtained written informed consent from the patients.

Study population

After obtaining informed consent, all patients scheduled for elective neurosurgery and having recovered in the PACU during the study period were divided into two groups, the Craniotomy Group (CG), and the Non-Craniotomy Group (NCG). We excluded patients who refused to participate in the study, those who do not speak or understand the language, patients who remained intubated postoperatively, and those who were transferred to the SICU for postoperatve care. In the CG we also excluded patients who underwent ventriculoperitoneal shunt or cranioplasty and, in the NCG, those who underwent subcutaneous internal pulse generator implant, cerebrospinal fluid (CSF) infusion test under sedation or patients who had previously undergone craniotomy.

Design and data collection

We collected the following demographic data: age, sex, the American Society of Anesthesiologists (ASA) physical status classification system, diagnosis, type of surgery, and anesthetic technique. We collected intraoperative data including blood loss greater than 1000 mL, hemodynamic instability requiring the administration of vasoactive drugs (repeated doses or an infusion), the presence of relative hypoxemia for a given FiO_2 administered (PaO_2/FiO_2 ratio <250), anisocoria upon emergence, and death.

The main parameters registered were:

(a) Neurological assessment scales: size and reactivity of the pupils, GCS, Ramsay scale, CNS, and the Nu-DESC (Appendix A).
(b) BIS recording: BIS value, signal quality index (SQI), EMG and suppression ratio (SR). The BIS sensor was placed on the contralateral side of the craniotomy. In posterior fossa craniotomy surgery and in the NCG, the BIS were placed in the dominant hemisphere to standardize the measurement. In each patient, we used the same BIS sensor for all BIS recordings. In cases of poor signal quality, the sensor was repositioned on the same side until an adequate signal was obtained. All BIS measurements were recorded before any neurological evaluation.
(c) Postoperative neurological complications. Neurological complications were defined as any clinically significant neurological alteration documented in the patient's medical record during their time in the PACU, in the neurosurgical ward, and any computed tomography and/or magnetic resonance imaging (CT-MRI) finding considered as a complication according to the neurosurgeon criteria.
(d) Follow-up: after discharge, any visit to the emergency department or readmission was recorded during the first postoperative month.

The time data recorded were: T0 – baseline, patient arrival at the pre-anesthesia before administration of premedication; Ta – patient admission to the PACU after surgery, once stabilized; T1, T2 – records in each nursing shift, Td – PACU discharge to the neurosurgical ward (Fig. 1). We also recorded any episodes with BIS < 70 maintained for 1 min after admission to the PACU, regardless of time of study.

We defined as altered neurologic scales the following criteria: anisocoria and/or loss of pupillary reactivity; GCS < 15 except GCS = 14 with ocular response = 3; Ramsay scale 1 or ≥4; CNS < 10, except CNS = 8.5 with level of consciousness = 1.5; Nu-DESC > 0. We excluded those patients with GCS = 14 (ocular response = 3) and CNS = 8.5 (level of consciousness = 1.5) because these scores might be due to residual effects of anesthesia or analgesic effects of opioids. We defined as altered BIS a BIS value below 70 for

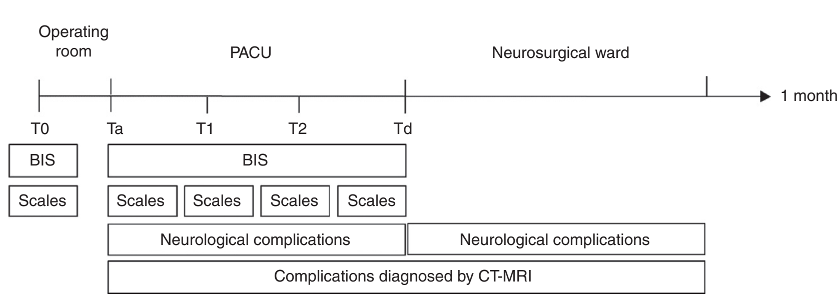

Figure 1 Chronogram of the study (PACU, post anesthesia care unit; T0, basal; Ta, admission to the PACU; T1 and T2, records in each nursing shift; Td, discharge to the neurosurgical ward; BIS, Bispectral Index; Scales, neurological scales applied; CT-MRI, computerized tomography-magnetic resonance imaging).

1 min. It was not considered an alteration if the value of the neurological scale or the BIS was already abnormal at baseline.

We defined as altered pupils-GCS or altered scales-BIS if at least one of the assessments (pupils, GCS or pupils, GCS, Ramsay scale, CNS, Nu-DESC, BIS) was altered according to our definition.

When an abnormality in a neurological assessment scales was observed, the anesthesiologist in charge of the patient's care would proceed to treat the patient according to the established protocols in each case.

We compared BIS among patients with and without postoperative neurological complications and we did an analysis to see if there was a BIS threshold able to predict the presence of postoperative neurological complications.

We analyzed the concordance between altered neurologic scales and altered BIS and the concordance between altered neurologic scales or altered BIS and the occurrence of neurological complications in PACU, in the ward, and abnormalities diagnosed on the CT-MRI. We also analyzed the ability of the altered pupils-GCS and altered scales-BIS assessments to identify neurological complications in the PACU. Finally we studied estimates of risk for the occurrence of postoperative neurological complications.

Statistical analysis

For the analysis of demographic data, age was expressed as mean ± standard deviation (SD) and analyzed with *t* test for independent groups. Categorical variables such as sex and ASA, were expressed in absolute values (valid percentage) and were analyzed using Chi-square or the Fisher exact test and Mann–Whitney *U* test for ordinal variables, as ASA. The BIS, SQI and EMG values were expressed as median and interquartile range (IQR). The analysis of BIS, SQI and EMG between each recording time from baseline test was performed using the Wilcoxon signed ranks. For analysis of differences between groups at each time of registration, we applied the Mann–Whitney *U*. The analysis of differences in BIS values between postoperative neurological complicated and uncomplicated patients was done with Mann–Whitney *U* test. The receiver operating characteristic (ROC) curve was used to determinate if, globally, the BIS had a predictive value for the occurrence of postoperative neurological complications and we calculated the likelihood ratio positive (LR+),[18] defined as ratio sensitivity/(1-especificity), for possible candidates of a BIS cut-off value. We performed a binary logistic regression analysis in order to obtain estimates of risk for the occurrence of postoperative neurological complications by calculating odds ratios (OR) and 95% confidence intervals (95% CI) of the altered neurological scales and BIS.

The Cochran *Q* test was used for the intragroup analysis of the differences between the times of recording of altered neurologic scales and altered BIS. The McNemar's test was applied for comparison between data recording times and baseline data. The Fisher exact test was used to compare the proportions of alterations in the neurologic scales and the BIS between CG and NCG. Comparisons between altered GCS-pupils and altered scales-BIS were performed using the McNemar test.

Analysis of concordance between alterations in the neurological assessment scales or BIS and the occurrence of postoperative neurologic complications was performed using Kappa index according to Landis & Koch criteria.[19] We considered a poor concordance if kappa values were less than 0, slight between 0 and 0.20, fair between 0.21 and 0.40, moderate between 0.41 and 0.60, substantial between 0.61 and 0.80 and almost perfect between 0.81 and 1. We calculated sensitivity, specificity, positive and negative predictive values of altered pupils-GCS and altered scales-BIS to identify neurological complications in the PACU. We considered significant *p*-values ≤ 0.05 and Bonferroni correction was used when indicated. Analyses were performed with the use of SPSS software (version 18.0, SPSS Inc., Chicago, IL, USA).

Results

Of the 151 patients who met inclusion criteria during the study period, we analyzed a total of 116 patients, 70 in the CG and 46 in the NCG. Nineteen patients were excluded in the CG and 16 patients in the NCG (Fig. 2).

Subjects demographic and clinical characteristics

CG patients were at higher preoperative risk and the NCG patients were older. In both groups, intravenous anesthesia was the technique most commonly used: 67 (95.7%) in CG and 45 (97.8%) in NCG. In 3 cases (4.3%) the anesthetic technique was conscious sedation (CG) and in 1 case (2.2%) inhalation anesthesia (NCG). Intraoperative complications occurred in 16 cases (22.9%) in CG and 4 cases (8.7%) in NCG (Table 1).

CG patients remained in the PACU an average of 16.5 ± 5.6 h, 57 of them (81.4%) spent the first postoperative night in the PACU (19.1 ± 1.6 h) while 13 (18.6%) were transferred to the ward the same day of surgery (5.6 ± 1.1 h). In the NCG group, the average PACU stay was 5 ± 5.4 h. Four patients (8.7%), 3 spinal cancer tumor resection and 1 cervical microdiscectomy, spent the first postoperative night in the PACU (20.1 ± 2.8 h), 42 (91.3%) were transferred from the PACU to the ward after recovering from anesthesia (3.6 ± 2.6 h). In NCG only 4 patients who stayed overnight in the PACU had data recorded at times T1 and T2.

BIS recordings

BIS values were significantly decreased upon PACU admission when compared to baseline in the CG ($p < 0.001$) and NCG ($p = 0.002$). The SQI remained above 70, except at discharge on NCG (SQI = 57.5). In both groups, the SQI at discharge decreased significantly compared to baseline ($p < 0.001$). EMG was below 50 at every recorded time in both groups. In the NCG, EMG value increased significantly upon PACU admission when compared to baseline ($p = 0.001$) (Fig. 3). SR was 0 in all patients. In 16 CG patients and only one patient in the NCG there were recorded episodes with BIS values <70 maintained for one minute during admission in the PACU.

In the CG group, we found differences in BIS values at T0 between patients who did not develop complications on CT-MRI (median = 94, IQR = 8) and those who did (median = 84, IQR = 10.5) ($p = 0.016$), and in BIS values at T2 between

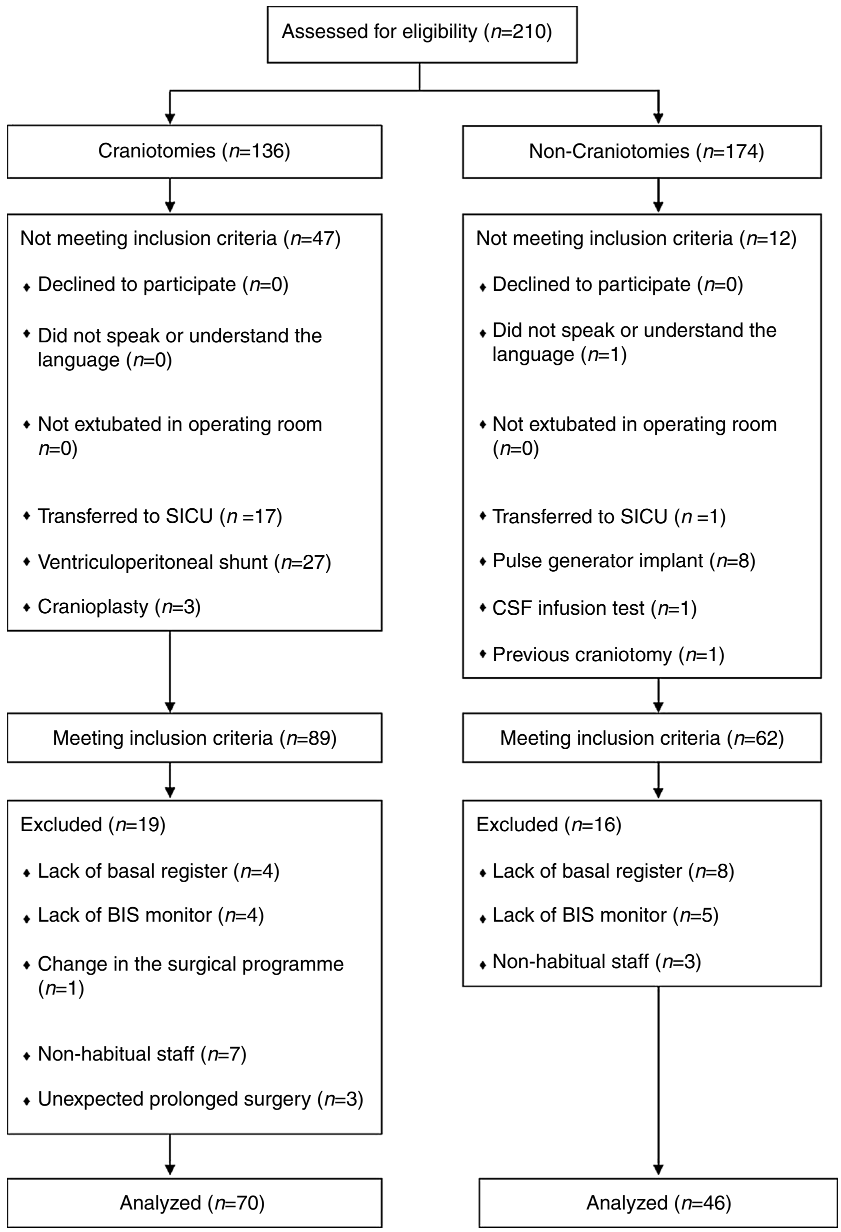

Figure 2 Study flow chart (SICU, surgical intensive care unit; CSF, cerebrospinal fluid; BIS, bispectral index).

patients who did not develop complications in the ward (median = 93, IQR = 12) and those who did (median = 82, IQR = 16) ($p = 0.019$). The ROC curve showed that the measured values of T2 BIS could predict the occurrence of neurological complications in the ward ($p = 0.019$; area under the curve 0.743, 95% CI = 0.566–0.920), with the BIS of 90 resulting in a LR+ for complication of 3.8 from a sensitivity value of 69% and specificity of 81.8%.

Alterations in the neurological evaluation scales and BIS

The pupils-GCS assessment was altered in the CG in 14 cases (20%) and the scales-BIS in 36 cases (51.4%) ($p < 0.001$). In the NCG we registered altered pupils-GCS in 1 case (2.2%) and altered scales-BIS in 18 cases (39.1%) ($p < 0.001$) (Table 2). In the CG, we found a moderate concordance between altered BIS and altered GCS ($\kappa = 0.438$; $p = 0.001$) and a fair concordance between altered BIS and altered Nu-DESC ($\kappa = 0.345$; $p = 0.008$) and altered BIS and altered Ramsay ($\kappa = 0.260$; $p = 0.029$).

Postoperative neurological complications

In the PACU, 16 patients (13.8% of total) had neurological complications, all in the CG group (22.9% of the CG) (Table 3). Aphasia was the most common complication (5.7%). In only 3 cases, an urgent CT was indicated in the PACU. In the first case, the indication for was anisocoria. The CT scan showed a pneumocephalus with mass effect. In the PACU, anisocoria (3/5) persisted and altered Ramsay (1 at Td) and altered BIS values, between 53 and 64,

Table 1 Demographic and clinical characteristics of the subjects.

Variable	Total (*n* = 116)	CG (*n* = 70)	NCG (*n* = 46)	*p*
Age, years, mean ± SD	54 ± 16.5	51.1 ± 16.5	58.5 ± 15.7	0.018
Sex, women, *n* (%)	69 (59.5)	43 (61.4)	26 (56.5)	0.6
ASA, *n* (%)				<0.001
ASA I	10 (8.6)	0 (0.0)	10 (21.7)	<0.001
ASA II	68 (58.6)	39 (56.7)	29 (63)	0.435
ASA III	38 (32.8)	31 (44.3)	7 (15.2)	0.001
Intervention, *n* (%)				
Supratentorial		24 (34.3)		
Transsphenoidal		20 (28.6)		
Posterior fossa		12 (17.1)		
Functional surgery		11 (15.7)		
Other craniotomies		3 (4.3)		
Lumbar microdiscectomy			16 (34.8)	
Lumbar laminectomy			12 (26)	
Spinal tumor			5 (10.9)	
Cervical microdiscectomy			4 (8.7)	
Brachial plexus surgery			4 (8.7)	
Cervical laminectomy			3 (6.5)	
Other			2 (4.4)	
Intraop. Complications, *n* (%)	20 (17.2)	16 (22.9)	4 (8.7)	0.074
Hemodynamic instability	11 (9.5)	9 (12.9)	2 (4.3)	0.196
Bleeding	7 (6)	5 (7.1)	2 (4.3)	0.704
Anisocoria	2 (1.7)	2 (2.9)	0 (0)	0.522
Hypoxemia	1 (0.9)	1 (1.4)	0 (0)	1.000
Mortality	0 (0)	0 (0)	0 (0)	–

CG, Craniotomy Group; NCG, Non-Craniotomy Group; ASA, American Society of Anesthesiologists; SD, standard deviation. The same patient could develop several complications.

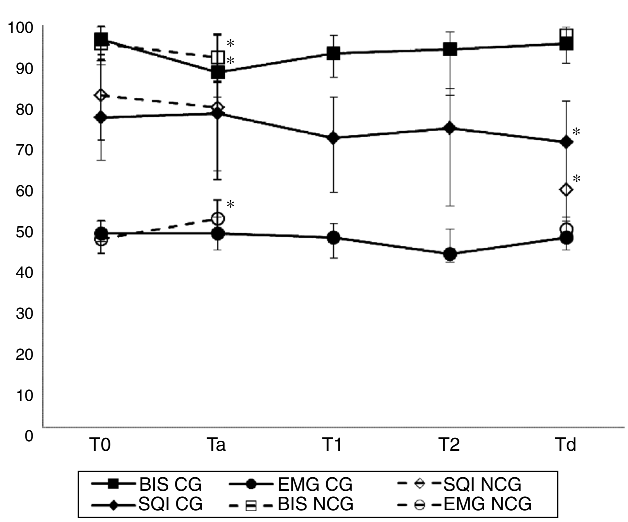

Figure 3 Changes in bispectral index records during the postoperative period (Data expressed as median and interquartile range (bars). T0, basal; Ta, admission to the post-anesthesia care unit (PACU); T1 and T2, records in each nursing shift (only in CG); Td, discharge to the neurosurgical ward; BIS, Bispectral Index; SQI, signal quality index; EMG, electromyogram; CG, craniotomy group (closed symbols); NCG, non-craniotomy group (open symbols). *Significant differences compared to T0 value in each group).

were registered. In the second case, a CT was requested for expressive aphasia and a reduced GCS, showing a large pneumocephalus. There were alterations in the pupils, the Ramsay scale, the CNS, the Nu-DESC and the BIS. An urgent CT was requested in the third case after a worsening aphasia was noted and it also showed a pneumocephalus. The neurological examination showed alterations in GCS, Ramsay, CNS, Nu-DESC and BIS values between 33 and 55. Three of the 5 patients who bled intraoperatively more than 1000 mL showed neurological complications in the PACU (aphasia, agitation, anisocoria). In all three cases the neurological scales were altered.

In the ward, a total of 23 patients (19.8%) suffered neurological complications, 18 (25.7%) in the CG and 5 (10.9%) in the NCG (Table 3). Cranial nerve palsy was the most common complication in the CG group (7.1%) and sciatic pain in NCG (4.3%). In the CG, one patient developed bradypsychia. The CT scan showed a pneumocephalus. During his stay in the PACU, the patient had altered GCS, CNS and Nu-DESC. Another patient developed absence seizures with a normal CT. We defined absence seizures in this patient as lapses of awareness episodes lasting only a few minutes and consisting of a decrease in the level of consciousness, lack of visual contact, decrease in reactivity, low breathing rate with deep inspirations and stereotyped limb movements. Unfortunately, an EEG could not be recorded during the events but simultaneous recording of BIS showed a decrease of BIS

Table 2 Alterations in the neurological evaluation scales and BIS in the post anesthesia care unit.

Group	Total time in the PACU, *n* (%)	T0, *n* (%)	Ta, *n* (%)	T1, *n* (%)	T2, *n* (%)	Td, *n* (%)	p[a]
Pupils							
CG (n = 70)	6 (8.6)	1 (1.4)	4 (5.7)	5 (8.6)	4 (9.8)	5 (7.2)	0.236
NCG (n = 46)	0 (0)	0 (0)	0 (0)			0 (0)	
p[b]	0.080	0.423	0.154			0.155	
GCS							
CG (n = 70)	10 (14.3)	1 (1.4)	8 (11.6)	3 (5.2)	4 (9.8)	5 (7.2)	0.038
NCG (n = 46)	1 (2.2)	0 (0)	1 (2.2)			0 (0)	1.000
p[b]	0.048	0.418	0.083			0.082	
Ramsay							
CG (n = 70)	13 (18.6)	2 (2.9)	6 (8.6)	6 (10.3)	5 (12.2)	5 (7.2)	0.669
NCG (n = 46)	5 (10.9)	1 (2.2)	5 (10.9)			0 (0)	0.063
p[b]	0.305	0.821	0.751			0.082	
CNS							
CG (n = 70)	18 (25.7)	6 (8.6)	14 (20.3)	9 (15.8)	7 (17.1)	9 (13)	0.159
NCG (n = 46)	13 (28.3)	16 (34.8)	10 (21.7)			7 (15.2)	0.508
p[b]	0.831	<0.001	1.000			0.787	
Nu-DESC							
CG (n = 70)	10 (14.3)	6 (8.6)	7 (10)	7 (12.1)	6 (16.2)	5 (7.2)	0.186
NCG (n = 46)	1 (2.2)	2 (4.3)	1 (2.2)			0 (0)	1.000
p[b]	0.048	0.382	0.144			0.082	
BIS							
CG (n = 70)	16 (23.2)	0 (0)	2 (3)	2 (3.7)	3 (7.5)	0 (0)	0.162
NCG (n = 46)	1 (2.2)	0 (0)	0 (0)			0 (0)	
p[b]	0.002	1.000	0.513			1.000	
Pupils-GCS							
CG (n = 70)	14 (20)	1 (1.4)	11 (15.9)	8 (13.8)	7 (17.1)	9 (18)	0.002
NCG (n = 46)	1 (2.2)	0 (0)	1 (2.2)			0 (0)	0.368
p[b]	0.008	1.000	0.026			0.011	
Scales-BIS							
CG (n = 70)	36 (51.4)	11 (15.7)	23 (34.3)	23 (42.6)	16 (43.2)	18 (27.7)	0.001
NCG (n = 46)	18 (39.1)	17 (37)	14 (30.4)			7 (15.6)	0.025
p[b]	0.254	0.014	0.689			0.168	

BIS, Bispectral Index; PACU, Post Anesthesia Care Unit; GCS, Glasgow Coma Scale; CNS, Canadian Neurological Scale; Nu-DESC, Nursing Delirium Screening Scale; Pupils-GCS, alteration in pupil and/or GCS; Scales-BIS, alteration in any of the neurological assessment scales and/or BIS; CG, Craniotomy Group; NCG, Non-Craniotomy Group; T0, basal; Ta, admission in the PACU; T1 and T2, records in each nursing shift; Td, discharge from the PACU.

[a] p within group (time) comparison.

[b] p between group comparison.

value up to 38 (EMG 28, SQI 96, SR 0). Prodromal symptoms included nausea and hyperventilation. An EEG recorded 24 h later, when the patient was asymptomatic, showed a left fronto-temporal continuous delta-theta slowing without any associated clinical changes. This neurological alteration was reported as ''absence seizure with an altered respiratory pattern'' in the patient's medical record. In the PACU, besides alterations in BIS, he also showed altered GCS, Ramsay score and Nu-DESC. One patient (cerebral lymphoma) died from septic shock. In the CG, 5 urgent CT's were requested on the ward: 4 for severe headache (3 with pneumocephalus), and 1 for seizures (pneumocephalus). In 4 of the 5 urgent CT's cases, impaired neurologic assessment scales were registered in the PACU. In the NCG, one patient developed paraplegia. The CT scan showed spinal cord compression from a massive hematoma. The patient underwent surgery again, but remained with residual paraparesis and required a permanent indwelling urinary catheter. During his stay in the PACU, neurological assessment scales and BIS were not altered. A patient with Neuro-Behçet disease was scheduled for decompression of the sciatic nerve and gluteal tumor excision (lymphoma). After starting chemotherapy, he was transferred to the ICU where he died of multiple organ failure two weeks after surgery.

Regarding complications diagnosed by neuroimaging, the neurosurgeon reported an abnormality in 11 cases (9.5%): 9 cases (12.9%) in the CG group and 2 (4.3%) in the NCG (Table 3). Seven patients in the CG had tension pneumocephalus (including urgent CT in the PACU or the ward). In the NCG, CT showed a cord compression in 2 patients, both

Table 3 Postoperative neurological complications.

CG (*n* = 70)			
Number of patients (%) with neurological complications in the PACU			
Total	16 (22.9)		
Aphasia	4 (5.7)	Agitation	1 (1.4)
Anisocoria	3 (4.3)	Psychomotor retardation	1 (1.4)
Headache	2 (2.9)	Dysarthria	1 (1.4)
Hipoesthesia	2 (2.9)	Nonconvulsive seizures	1 (1.4)
Cranial nerve palsy	2 (2.9)	Hemiplegia	1 (1.4)
Low level of consciousness	1 (1.4)	Paresis	1 (1.4)
Hallucination	1 (1.4)	Trigeminal neuralgia	1 (1.4)
Anxiety	1 (1.4)		
Number of patients (%) with neurological complications in the ward			
Total	18 (25.7)		
Cranial nerve palsy	5 (7.1)	Bradypsychia	1 (1.4)
Headache	4 (5.7)	Dystonia	1 (1.4)
Aphasia	4 (5.7)	Alexia	1 (1.4)
CSF fistula	4 (5.7)	Right-hemisphere Synd.	1 (1.4)
Seizures	2 (2.9)	Psychiatric decompensation	1 (1.4)
Number of patients (%) with neurological complications by CT-MRI			
Total	9 (12.9)		
Pneumocephalus mass effect	7 (10)	Infection	1 (1.4)
Hematoma mass effect	1 (1.4)		
NCG (*n* = 46)			
Number of patients (%) with neurological complications in the PACU			
Total	0 (0)		
Number of patients (%) with neurological complications in the in the ward			
Total	5 (10.9)		
Lumbosciatalgia	2 (4.3)	Unstable gait	1 (2.2)
Paraplegia	1 (2.2)	Disorientation	1 (2.2)
Number of patients (%) with neurological complications by CT-MRI			
Total	2 (4.3)		
Spinal cord compression	2 (4.3)		

CG, Craniotomy Group; NCG, Non-Craniotomy Group; PACU, Post Anesthesia Care Unit; CT-MRI, computed tomography-magnetic resonance imaging; CSF, cerebrospinal fluid. The same patient could develop more than one complication. Complications in the PACU, in the ward and by CT-MRI were not additive.

required an additional operation: one from a residual tumor and the other from a hematoma (patient with paraplegia detected in the ward).

During the first month after surgery 20 patients (17.2%) went to the emergency room or were readmitted to the hospital: 17 (24.3%) in the CG and 3 (6.5%) in NCG ($p = 0.014$). In the CG group the most common cause of readmission was a CSF fistula-5 cases (7.1%). In CG group 8 patients (11.4%) underwent second or repeat surgery: 5 (7.1%) for CSF leaks, 2 (2.9%) for surgical wound infection and 1 (1.4%) for epistaxis. In the NCG one patient was treated for neuropathic pain, another for lumbosciatalgia and the third for paralytic ileus. None required further surgery.

Concordance between alterations in neurological assessment scales or BIS and postoperative neurological complications

In the CG group, we found moderate concordance between alterations of GCS and the occurrence of neurological complications in the PACU and fair concordance between alterations of the Ramsay scale, CNS, Nu-DESC or BIS and the occurrence of neurological complications in the PACU. Alterations in CNS scores showed moderate concordance with abnormalities seen on the CT-MRI, alterations in GCS showed fair concordance. Equally, altered pupils-GCS and scales-BIS showed moderate and fair concordance, respectively, with neurological complications in the PACU (Table 4). In the NCG, we could not analyze concordance in most cases, because at least one of the variables remained constant.

Predictive values

The sensitivity and negative predictive value of the scales-BIS assessment to detect neurological complications in the PACU in the CG was greater than the pupils-GCS assessment (94% vs. 50% and 97% vs. 86%, respectively), and with a lower specificity (61% vs. 89%) and positive predictive value (42% vs. 57%).

Table 4 Analysis of concordance between alterations in neurological assessment scales or bis and occurrence of postoperative neurological complications in craniotomy group.

	Complications in the PACU		Complications in the ward		Complications diagnosed by CT-MRI	
	Kappa	*p*	Kappa	*p*	Kappa	*p*
Pupils	0.169	0.098	0.044	0.655	0.000	0.250
GCS	0.440	<0.001	0.213	0.058	0.399	0.006
Ramsay	0.263	0.027	0.136	0.244	0.143	0.326
CNS	0.379	0.001	0.177	0.138	0.530	<0.001
Nu-DESC	0.347	0.003	0.213	0.058	0.175	0.229
BIS	0.349	0.004	0.220	0.066	0.108	0.460
Pupils-GCS	0.407	0.001	0.274	0.020	0.240	0.097
Scales-BIS	0.381	<0.001	0.155	0.133	0.161	0.132

Craniotomy Group ($n = 70$). BIS, Bispectral Index; PACU, Post Anesthesia Care Unit; CT-MRI, computed tomography-magnetic resonance imaging; GCS, Glasgow Coma Scale; CNS, Canadian Neurological Scale, Nu-DESC, Nursing Delirium Screening Scale, Pupils-GCS, alteration in pupil and/or GCS; Scales-BIS, alteration in any of the neurological assessment scales and/or BIS.

Odds ratio of altered neurological scales and BIS for postoperative neurological complications

In the CG, altered pupils, GCS, CNS, pupils-GCS and scales-BIS were estimates of risk for postoperative neurological complications. On admission to the PACU, the scales-BIS assessment allowed a more precise estimate for the occurrence of neurological complications in the PACU (Table 5). In the NCG, the probability of developing neurological complications in the ward among patients with altered CNS on admission to the PACU was 7.28 times of those with non-altered CNS ($p = 0.048$; 95% CI = 1.021–52.006).

Table 5 Significant odds ratio of altered neurological scales and BIS for the occurrence of postoperative neurological complications in craniotomy group.

Time	Diagnosis of neurological complication	Odds ratio	95% CI	*p*
Pupils				
Ta	PACU	12.23	1.18–127.36	0.036
GCS				
Ta	PACU	7.58	1.57–36.53	0.012
Td	Ward	15.69	1.61–152.55	0.018
Td	CT-MRI	18.00	1.60–202.95	0.019
Ta, T1, T2 and Td	CT-MRI	9.33	1.59–54.58	0.013
CNS				
Ta	PACU	5.11	1.44–18.16	0.012
Td	Ward	8.91	1.92–41.24	0.005
Ta	CT-MRI	10.31	1.93–59.05	0.006
Td	CT-MRI	9.07	1.55–53.07	0.014
Ta, T1, T2 and Td	CT-MRI	18.67	3.09–112.61	0.001
Pupils-GCS				
Ta	PACU	9.53	2.31–39.39	0.002
Td	Ward	8.91	1.92–41.24	0.005
Ta, T1, T2 and Td	Ward	4.09	1.19–14.11	0.026
Scales-BIS				
Ta	PACU	7.15	2.07–24.69	0.002
Ta	Ward	3.40	1.06–10.88	0.039
Ta	CT-MRI	5.78	1.19–28.04	0.030

Craniotomy Group ($n = 70$); BIS, Bispectral Index; GCS, Glasgow Coma Scale; CNS, Canadian Neurological Scale; Pupils-GCS, alteration in pupil and/or GCS; Scales-BIS, alteration in any of the neurological assessment scales and/or BIS; PACU, post-anesthesia care unit; T0, basal; Ta, admission in the PACU; T1 and T2, records in each nursing shift; Td, discharge from the PACU; CT-MRI, computed tomography-magnetic resonance imaging; CI, confidence interval.

Discussion

The scales-BIS assessment let us detect a high percentage of neurological alterations that were not detected using the traditional evaluation pupils-GCS. In the CG, that fact confirms that after craniotomy, patients have an increased risk of neurological complications in the immediate postoperative period. Detecting these disturbances allows early diagnostic or therapeutic interventions that can decrease postoperative neurologic complications and improve prognosis.[8] In our study, all patients who needed an urgent CT in the PACU had altered neurological assessment scales. We believe that our results support the use of a more complete neurological assessment rather than the simple analysis of pupils and GCS.

Benefits and limitations of BIS

BIS could be useful as an additional tool to predict the occurrence of neurological postoperative complications, but probably not beyond other well know methods. The study demonstrates that the standard perioperative assessment tools of GCS and careful neurologic examination proved effective to identify clinically significant complications, regardless of BIS recordings. The BIS is a continuous monitoring that has to alert us for a more exhaustive neurological assessment. Clinical examination and BIS do not have to be mutually exclusive but complementary tools. BIS monitoring was feasible in the postoperative period in extubated patients. High values of SQI, although the EMG could not be less than 40, support the fact that these were reliable recordings. The residual anesthetic effect could explain the decrease in BIS values when the patient was admitted to the PACU, as BIS began recovering shortly afterwards. Our neurologic assessment scales included direct or indirect assessment of the level of consciousness, although, each scale assigning a different specific value. That could explain the agreement between altered BIS and altered neurological assessment scales. However, we found no association between BIS alterations and alterations of the Ramsay scale. Other studies have found similar results when EMG recordings were above 30.[20] On the other hand, we also found that altered BIS was associated with the occurrence of neurological complications in the PACU. Interestingly, we found significant differences in basal BIS values (T0) between patients who did and who did not develop neurological complications by CT-MRI. This result may suggest that basal BIS could be a potential risk factor of postoperative neurological complications associated with CT-MRI abnormalities in patients scheduled for craniotomy. However, this is an isolated result in a small sample of patients and it does not allow us to make any valid conclusion. In a recent study in patients with delayed awakening after craniotomy, the cerebral state index monitoring, a monitor that analyses electroencephalogram tracing similarly to the BIS, proved to have a high prediction probability for long-term unconsciousness (>24 h) when the measured values in the first 6 h postoperatively was below 54–63.[21] We could not analyze whether the BIS was a better predictor of neurological complications associated with a decreased level of consciousness, because the number of these events was too low. In addition, our criteria to define the BIS alteration (BIS < 70 for 1 min) might be too demanding, according to the results of the ROC curve. It remains to be studied whether the BIS better predicts the impaired consciousness in patients after craniotomy and what cut off value in the BIS might provide the highest predictive probability. Nevertheless, the introduction of a BIS scale is subject to limitations as EMG activity or filtering effect of air in the subarachnoid space. BIS has risks of raising an unwarranted alarm bells by virtue of its poor degree of specificity and could suggest nurses not to observe simple facts, such as level of consciousness and focal deficits that are evaluated in a clinical examination.

Association between altered neurological assessment scales or BIS and development of postoperative neurological complications – estimates of risk

Altered neurological assessment scales were associated with the development of postoperative neurological complications. A previous study showed that the level of awareness in postoperative patients with subarachnoid hemorrhage who underwent surgery was a good predictor of neurological outcome.[22] Other studies have found additional predictors of postoperative neurologic complications, including the duration of surgery, the surgical position, intraoperative bleeding, or the appearance of new neurological deficit after surgery.[23,24] We also found that most craniotomy patients with significant intraoperative bleeding showed postoperative neurologic complications in the PACU. We could find no previous studies comparing neurological assessment scales in patients after craniotomy to best predict the occurrence of neurologic complications. We found that, independently, the GCS and CNS were the most precise estimates of risk. GCS is well-known to predict neurologic outcome in head injury and subarachnoid hemorrhage.[25] The CNS in turn allows more subtle abnormalities of motor function, which probably explains why this scale detected the most alterations in both groups. Our results also show that traditional examination of the pupils and the GCS is useful to estimate the occurrence of postoperative neurological complications, but, probably, not enough. Iacono et al.,[26] introduced The Basic Neurological Check for use on any patient with a confirmed or suspected neuroscience diagnosis, except stroke. This tool included assessment of orientation, ability to follow commands, motor strength and assessment for facial droop. Although no formal process was conducted to evaluate its effectiveness, nurses verbalize more confidence in their ability to identify clinical symptoms promoting early diagnosis and treatment. Complete neurological examination with assessment of the Ramsay scale, CNS, Nu-DESC and BIS helps to improve this estimate. The high sensitivity of the scales-BIS assessment suggests that if a preliminary screening of the population at risk of developing postoperative neurological complications was made, probably, the predictive accuracy of the assessment would increase.

We were surprised by the number of patients in which the Nu-DESC was altered, even at baseline. General anesthesia and neurosurgery by themselves are probably the main causes of the occurrence of disorientation, inappropriate behavior, inappropriate communication, illusions/hallucinations or psychomotor retardation in the postoperative period. The main mechanism seems to be associated with altered synaptic neurotransmission induced by anesthesia or brain damage due to surgical trauma, ischemia, edema, etc. Probably, the use of a specific scale for assessing these alterations would help to detect them. On the other hand, we considered any alteration in the scale as an alert signal although did not exceed the cut off diagnosis of delirium according to the original scale.[11]

An interesting finding was the ability of neurological assessments at admission and discharge from the PACU to predict the appearance of postoperative neurological complications. Based on our results, the presence of abnormal scales-BIS on admission to the PACU or the presence of altered pupils-GCS or altered CNS at discharge from the PACU would be good indicators for recommending longer surveillance and patient monitoring. Eighty one percent of our patients underwent overnight monitoring after elective craniotomy but only 34% had altered scales-BIS at admission to the PACU and 31% altered pupils-GCS or CNS at discharge. The level of care after an elective craniotomy is a matter of concern. Identifying predictors for postoperative neurological complications could be useful to select patients who require a more intensive level of observation and monitoring. Several publications show some preoperative and intraoperative predictors: Hanak et al.[27] found diabetes and older age to be predictive for postoperative ICU admission. In a neurosurgical patient population, the application of the surgical Apgar score, based on the estimated blood loss, the lowest intraoperative mean arterial blood pressure and the lowest heart rate predicted 30 day postoperative mortality, complication rate, prolonged ICU and hospital stay. The authors stated this score may be useful to efficiently plan postoperative care.[28] Wanderer et al.[29] developed and validated an intraoperative predictive model for unplanned postoperative intensive care unit admission that may improve the process of allocating intensive care unit beds postoperatively. In this regard, our study adds the potential usefulness of applying neurological assessment scales and BIS in the PACU.

Limitations of the study

We were aware of some limitations of the study. First, both the patients and the nursing staff in the PACU knew about this study. Second, we excluded the more seriously ill patients (patients intubated or discharged to the SICU) because the present study focused on patients' extubated in the operating room and who remained in the PACU postoperatively. Third, it was impossible to obtain BIS values with EMG activity <30. The extubated neurosurgical patient in the PACU, unlike the intubated patient, does not require pharmacological sedation making it more difficult to decrease the EMG activity. However, the quality of the sign obtained was appropriate. Fourth, our criteria for defining neurological complications were based on medical reports and the neurosurgeon's assessment of CT-MRI. While some authors have used stricter criteria (well-defined neurologic impairment, precise imaging abnormalities, or specific neurological interventions),[24] in other cases the criteria is broader when defining neurological complications (postoperative new deficits).[23] Finally, patients in the CG and NCG were not comparable. The demographic and clinical differences are explained by the different nature of their surgical pathologies. While in the CG, the main pathology was neoplastic with great general status affectation, patients in the NCG had osteoarticular pathology, typical of older ages, resulting in more motor impairment. The higher incidence of intraoperative complications in the CG was due, probably, to increased preoperative surgical risk.

In summary, our study suggests that neurological assessment scales and BIS, independently and pooled, could be useful to predict the occurrence of neurological complications postoperatively. By adding assessments, the number of events detected was higher, the confidence interval decreased, and the estimates became more accurate. BIS does not substitute neurological clinical examination to identify clinically significant complications. We could not determine the scale or combination of scales that best estimates the occurrence of neurological complications. To find the best predictive model and the cut offs studies with a large number of patients and more complex logistic regression analysis is needed. It would also be interesting to investigate what neurological assessment scales are best for each different neurological complication, and whether these neurologic assessment scales and BIS are applicable to predict outcome in other procedures with a high risk of postoperative neurological complications, like cardiac or orthopedic surgery, or in neurocritical patients (subarachnoid hemorrhage, head injury, etc.).

Applied together, the assessment of pupils, GCS, Ramsay scale, CNS, Nu-DESC and BIS, improved early detection of postoperative neurological complications in PACU after elective craniotomies.

Conflicts interests

The authors declare no conflicts of interest.

Acknowledgements

The authors thank the Neurosurgery Service in our facilities as well as Dr. Victor Obach (Neurology Department) and Dr. Jordi Rumia (Neurosurgery Service) for their help determining which neurological scales were most appropriate for this study, the other members of the Post Neuroanesthesia Care Group[a] and the anesthesia residents for their help with data collection, Dr. Josep María Nicolas for his support, and to all the others in our institution that contributed and made this project possible.

[a] Post Neuroanesthesia Care Group: Marta Carme RN; Enrique Carrero MD, PhD; Isabel Cubero RN, MSN; Nicolás de Riva MD, Neus Fàbregas MD, PhD; Isabel Gracia MD; Silvia Herrero RN, MSc; Paola Hurtado MD; Dolores Pavon RN; Nuria Peix RN; Montse Sánchez RN, MSc; Francisco Javier Tercero MD; Ricard Valero MD, PhD.

Appendix A. Neurological assessment scales applied in the study

Pupil examination

Assessment		Score
Pupil size (left/right)	1 mm	1
	2 mm	2
	3 mm	3
	4 mm	4
	5 mm	5
Pupil reaction (left/right)	No reaction	0
	Reacts	1

Pupil anisocoria, pupils of different size; pupil no reaction, a pupil that does not contract when exposed to a bright light.

Glasgow Coma Scale (GCS)[4]

Category	Responses	Score
Eye opening	Spontaneously	4
	To speech	3
	To pain	2
	None	1
Verbal response	Orientated	5
	Confused	4
	Inappropriate	3
	Incomprehensible	2
	None	1
Motor response	Obeys commands	6
	Localizes to pain	5
	Withdraws from pain	4
	Flexion to pain	3
	Extension to pain	2
	None	1
Maximum score		15

Ramsay Scale[9]

Level of activity	Score
Patient anxious and agitated or restless or both	1
Patient co-operative, orientated, and tranquil	2
Patient responds to commands only	3
Patient exhibits brisk response to light glabellar tap or loud auditory stimulus	4
Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus	5
Patient exhibits no response	6

Canadian Neurological Scale (CNS)[10]

Mentation		Score
Level of consciousness	Alert	3.0
	Drowsy	1.5
Orientation	Oriented	1.0
	Disoriented/NA	0.0
Speech	Normal	1.0
	Expressive deficit	0.5
	Receptive deficit	0.0
	Total:	

Section A1	Motor functions	Weakness	Score
No comprehension deficit	Face	None	0.5
		Present	0.0
	Arm, proximal	None	1.5
		Mild	1.0
		Significant	0.5
		Total	0.0
	Arm, distal	None	1.5
		Mild	1.0
		Significant	0.5
		Total	0.0
	Leg, proximal	None	1.5
		Mild	1.0
		Significant	0.5
		Total	0.0
	Leg, distal	None	1.5
		Mild	1.0
		Significant	0.5
		Total	0.0
		Total:	

Section A2	Motor response	Weakness	Score
Comprehension deficit	Face	Symmetrical	0.5
		Asymmetrical	0.0
	Arms	Equal	1.5
		Unequal	0.0
	Legs	Equal	1.5
		Unequal	0.0
		Total:	

The Nursing Delirium Screening Scale (Nu-DESC)[11]

Symptom	Score (0–2)
I. Disorientation Verbal or behavioral manifestation of not being oriented to time or place or misperceiving persons in the environment	
II. Inappropriate behavior Behavior inappropriate to place and/or for the person; e.g., pulling at tubes or dressings, attempting to get out of bed when that is contraindicated, and the like	
III. Inappropriate communication Communication inappropriate to place and/or for the person; e.g., incoherence, noncommunicativeness, nonsensical or unintelligible speech	
IV. Illusions/hallucinations Seeing or hearing things that are not there; distortions of visual objects	
V. Psychomotor retardation Delayed responsiveness, few or no spontaneous actions/words; e.g., when the patient is prodded, reaction is deferred and/or the patient is unarousable	
	Total:

Symptoms are rated from 0 to 2 based on the presence and intensity of each symptom.

References

1. Fàbregas N. Complicaciones Neurológicas Perioperatorias. In: Gomar C, Villalonga A, Castillo J, Carrero E, Tercero FJ, editors. Formación Continuada en Anestesiología y Reanimación [Continuing medical education in anesthesiology and resuscitation], vol. 2. Madrid: Ergon; 2013. p. 739–47.
2. Beauchamp K, Baker S, McDaniel C, et al. Reliability of nurses' neurological assessments in the cardiothoracic surgical intensive care unit. Am J Crit Care. 2001;10:298–305.
3. Bickert AT, Gallagher C, Reiner A, et al. Nursing neurologic assessments after cardiac operations. Ann Thorac Surg. 2008;85:554–60.
4. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet. 1974;2:81–4.
5. Brott T, Adams HP Jr, Olinger CP, et al. Measurements of acute cerebral infarction: a clinical examination scale. Stroke. 1989;20:864–70.
6. Folstein MF, Folstein S, Mchugh PR. ''Mini-Mental State''. A practical method for grading the cognitive state of patients for the clinicians. J Psychiatr Res. 1975;12:189–98.
7. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Text revision (DSM-IV-TR), 4th ed. Washington DC: American Psychiatric Association; 2000.
8. Fàbregas N, Bruder N. Recovery and neurological evaluation. Best Pract Res Clin Anaesthesiol. 2007;21:431–47.
9. Ramsay MA, Savege TM, Simpson BR, et al. Controlled sedation with alphaxalone–alphadolone. Br Med J. 1974;2: 656–9.
10. Côté R, Battista RN, Wolfson C, et al. The Canadian Neurological Scale: validation and reliability assessment. Neurology. 1989;39:638–43.
11. Gaudreau JD, Gagnon P, Harel F, et al. Fast, systematic, and continuous delirium assessment in hospitalized patients: the Nursing Delirium Screening Scale. J Pain Symptom Manag. 2005;29:368–75.
12. Hodgate A, Ching N, Angonese L. Variability in agreement between physicians and nurses when measuring the Glasgow Coma Scale in the emergency department limits its clinical usefulness. Emerg Med Australas. 2006;18:379–84.
13. De Deyne C, Struys M, Decruyenaere J, et al. Use of continuous bispectral EEG to assess depth of sedation in ICU patients. Intensive Care Med. 1998;24:1294–8.
14. Adesanya AO, Rosero E, Wyrick C, et al. Assessing the predictive value of the bispectral index vs patient state on clinical assessment of sedation in postoperative cardiac surgery patients. J Crit Care. 2009;24:322–8.
15. Bruhn J, Bouillon TW, Shafer SL. Electromyographic activity falsely elevates the bispectral index. Anesthesiology. 2000;92:1485–7.
16. Riess ML, Graefe UA, Goeters C, et al. Sedation assessment in critically ill patients with bispectral index. Eur J Anaesthesiol. 2002;19:18–22.
17. Mondello E, Siliotti R, Noto G, et al. Bispectral index in ICU: correlation with Ramsay score on assessment of sedation level. J Clin Monit Comput. 2002;17:271–7.
18. Deeks JJ, Altman DG. Diagnostic tests 4: likelihood ratios. BMJ. 2004;329:168–9.
19. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;33:159–74.
20. Tonner PH, Wei C, Bein B, et al. Comparison of two bispectral index algorithms in monitoring sedation in postoperative intensive care patients. Crit Care Med. 2005;33:580–4.
21. Xu M, Lei YN, Zhou JX. Use of cerebral state index to predict long-term unconsciousness in patients after elective craniotomy with delay recovery. BMC Neurol. 2011;11:15.
22. Fàbregas N, Valero R, Carrero E, et al. Outcome of patients who underwent surgical repair of aneurysm after subarachnoid haemorrhage. Med Clin (Barc). 1998;111:81–7.
23. Kaakaji W, Barnett GH, Bernhard D, et al. Clinical and economic consequences of early discharge of patients following supratentorial stereotactic brain biopsy. J Neurosurg. 2001;94:892–8.
24. Rhondali O, Genty C, Halle C, et al. Do patients still require admission to an intensive care unit after elective craniotomy for brain surgery? J Neurosurg Anesthesiol. 2011;23:118–23.
25. Giraldo EA, Mandrekar JN, Rubin MN, et al. Timing of clinical grade assessment and poor outcome in patients with aneurysmal subarachnoid hemorrhage. J Neurosurg. 2012;117:15–9.
26. Iacono LA, Wells C, Mann-Finnerty K. Standardizing neurological assessments. J Neurosci Nurs. 2014;46:125–32.
27. Hanak BW, Walcott BP, Nahed BV, et al. Postoperative intensive care unit requirements after elective craniotomy. World Neurosurg. 2014;81:165–72.
28. Ziewacz JE, Davis MC, Lau D, et al. Validation of the surgical Apgar score in a neurosurgical patient population. J Neurosurg. 2013;118:270–9.
29. Wanderer JP, Anderson-Dam J, Levine W, et al. Development and validation of an intraoperative predictive model for unplanned postoperative intensive care. Anesthesiology. 2013;119:516–24.