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Validating the Sedation-Agitation Scale with the Bispectral Index and Visual Analog Scale in adult ICU patients after cardiac surgery

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Abstract *Objective*: To validate the Sedation-Agitation Scale (SAS) with the Visual Analog Scale (VAS) and Bispectral Index (BIS) in adult ICU patients after cardiac surgery.
Design: Prospective study comparing blinded evaluations of the SAS, VAS and BIS.
Setting: Forty-two-bed multidisciplinary ICU.
Patients and participants: Convenience sample of 39 adults after cardiac surgery.
Measurements and results: Bispectral Index 3.2 was continuously recorded using the Aspect A-1000 and evaluators were blinded to this value. The bedside nurse and a trained researcher independently rated wakefulness using a 100 mm VAS upon patient arrival on the ICU, at first awakening, when ventilator weaning was started and after extubation; the researcher also evaluated patients using SAS. Upon arrival on the ICU, the median SAS score was 2 (interquartile range = 1–3), the mean VAS was 26 ± 30 and the mean BIS was 70 ± 16. Twenty-four patients underwent a trial of weaning from mechanical ventilation with a SAS of 4 (IQR = 4), VAS of 86 ± 12 and BIS of 87 ± 10. SAS correlated well with VAS performed by one researcher ($r = 0.91$, $p < 0.001$) or by 19 different bedside nurses ($r = 0.43$, $p < 0.001$) and with BIS 3.2 ($r = 0.60$, $p < 0.001$). The correlation between SAS and BIS was reduced in patients with above average electromyogram (EMG) power. As a measure of construct validity, significant differences were noted for the BIS, SAS, VAS and EMG between ICU arrival and extubation (all $p < 0.001$).
Conclusions: Sedation-Agitation Scale and BIS are valid measures of wakefulness after cardiac surgery, but EMG interference may affect the accuracy of BIS for a small percentage of patients not receiving neuromuscular blockade.

Key words Conscious sedation · Intensive care unit · Psychomotor agitation · Reproducibility of results · Electroencephalogram · Bispectral index

Introduction

Many controversies surround the complex issue of patient sedation in the intensive care unit (ICU), including how to monitor or quantify sedation [1], what level of sedation is appropriate [2] and which medications and protocols are preferred [3, 4]. To allow us to compare the level of sedation and agitation attained by ICU patients, we previously developed and later refined the Sedation-Agitation Scale (SAS) [5, 6] (see Table 1). The SAS is a seven-point scale with progressive severity levels for both sedation and agitation, which has an excellent interrater reliability (weighted kappa = 0.92) and a strong correlation with the Ramsay score ($r = 0.91$) [6,

Table 1 Riker Sedation-Agitation Scale (SAS)

Score	Category	Description
7	Dangerous agitation	Pulling at endotracheal tube, trying to remove catheters, climbing over bedrail, striking at staff, thrashing side-to-side
6	Very agitated	Does not calm despite frequent verbal reminding of limits, requires physical restraints, biting endotracheal tube
5	Agitated	Anxious or mildly agitated, attempting to sit up, calms down on verbal instructions
4	Calm, cooperative	Calm, easily arousable, follows commands
3	Sedated	Difficult to arouse, awakens to verbal stimuli or gentle shaking but drifts off again, follows simple commands
2	Very sedated	Arouses to physical stimuli but does not communicate or follow commands, may move spontaneously
1	Unarousable	Minimal or no response to noxious stimuli, does not communicate or follow commands

7]. Both the SAS and Ramsay scores are subjective assessments which may not be reliable in the setting of neuromuscular blockade or sensitive during very deep sedation. The Bispectral Index (BIS), an electroencephalograph (EEG)-based objective scale from 0 (isoelectric EEG) to 100 (fully awake), correlates inversely with hypnotic drug effect [8]. In addition to power and frequency data derived from the fast Fourier transformation of the raw EEG, BIS incorporates features correlating with hypnotic drug effect derived from a large patient database [9]. The values for BIS are in the 90s for completely awake patients, drop into the 70s or 80s during conscious sedation, into the 50s and 60s during general anesthesia and below 40 during deep sedation or barbiturate coma. We have used the BIS to monitor a heterogeneous group of ICU patients and patients during fiberoptic bronchoscopy and found that BIS correlates with patient recall [10, 11]. Though not designed to test this agreement, our initial evaluation of ICU patients with the BIS showed a fair correlation with SAS ($r = 0.46$, $p < 0.001$) [11].

It is unclear how best to validate sedation scales, and a recent review of ICU sedation stated that no existing scale had been evaluated regarding ability to detect changes in sedation status over time [12]. Although many available scales have been compared with the Visual Analog Scale (VAS) as a clinimetric measure of wakefulness, the absence of a gold standard to monitor sedation in the ICU makes that type of criterion testing of validity imperfect [12, 13, 14]. When a gold standard is lacking, construct validity testing may be more appropriate [15]. Comparing the BIS to subjective assessments of sedation is complicated by the stimulation and increased wakefulness associated with the subjective assessment [11]; no standardized approach to this problem has been developed or tested.

In an effort to address many of these problems, we chose to study patient awakening in the ICU after cardiac surgery to allow serial monitoring over time using independent subjective assessment with SAS and VAS and blinded objective monitoring with the BIS. This model enables us to test the hypothetical construct that patients would have lower BIS, VAS and SAS scores on arrival at the ICU than at the time of extubation, and to develop a standard approach to determining the BIS relative to subjective scales.

Materials and methods

A convenience sample of patients arriving in the 42-bed ICU of Maine Medical Center (a 599-bed tertiary care hospital) after morning cardiac surgery were screened daily to identify one patient most likely to wean rapidly from the ventilator. We avoided enrolling patients with intra-aortic balloon pumps or other mechanical assist devices, difficulty separating from bypass, organ system failure, emergency surgery or any other significant perioperative (but pre-ICU) events which might delay extubation. Upon arrival on the ICU, patients were monitored with standard equipment including continuous electrocardiography and systemic and pulmonary artery catheters. Four EEG leads (Zipprep, Aspect Medical Systems, Newton, Mass.) were placed in a bilateral, two channel, fronto-temporal referential montage. Sedation and analgesia were administered by the bedside ICU nurse. We did not control selection of medications for sedation, but postoperative analgesia was provided using existing morphine- and fentanyl-based protocols. A standardized nurse and respiratory therapist driven ventilator weaning protocol guided this aspect of care in all cardiac surgery patients.

After placement of the EEG leads, impedance was determined to insure that lead-lead variability was minimal. If impedances differed by more than 2,500 ohms, the lead with the higher impedance was reapplied. Immediately after lead application and impedance evaluation, the entire display screen of the A-1000 bedside EEG monitor (Aspect Medical Systems, Newton, Mass.) was covered until the completion of the study period, obscuring all images of the BIS value and allowing all subjective assessments (SAS and VAS) to be performed blinded to the BIS. The BIS version 3.2 and power-spectrum derived EEG variables (95 % spectral edge, median frequency and relative power in the delta, theta, alpha and beta frequency ranges) and electromyographic (EMG) values were continually recorded by an in-line laptop computer. The visu-

Fig. 1 The Visual Analog Scale (VAS)

al analog scale (VAS) was assessed by drawing a perpendicular line along a 100 mm line bounded by the terms "very sedate" and "very alert" to identify the degree of sedation or wakefulness (see Fig. 1). The distance from the left end of the line to the perpendicular mark was measured in millimeters [13]. A single researcher performed the VAS, blinded to BIS values, four times: as soon as possible after arrival on the ICU and placement of the EEG leads (Time 1), at the time of first awakening (when patients first answered questions or followed commands – Time 2), at the start of ventilator weaning (Time 3) and immediately after extubation (Time 4). The SAS score was also assessed and entered into the laptop computer by a single trained investigator blinded to the BIS values. The bedside nurse (blinded to the values of the BIS and the researcher's assessments of SAS and VAS) independently assessed the VAS score the first three times. Patients were monitored until extubation or for the first 6 h after arrival in the ICU if still intubated.

We have identified, in previous studies, that the verbal and physical stimuli associated with subjective assessment of patients increase patient wakefulness with an accompanying increase in BIS values above baseline [11]. It is not clear which BIS value (pre-stimulation, post-stimulation or an average of the two) should be compared to the subjective assessments, but previous work suggests that an average value may be most appropriate [11]. The BIS score and other EEG variables were downloaded to the laptop every 30 s and the two EEG data sets recorded during the first minute of SAS assessment were averaged to obtain the value of the EEG-based variables corresponding to that specific SAS assessment.

Although the impact of the EMG on BIS values has been reported before [16], methods to assess this interaction have not been standardized. As an initial approach, the EMG signal was obtained from the EEG leads as the absolute power occurring in the frequency range from 70–110 Hz. We identified the mean EMG power of our patient cohort measured in decibels (dB) for all time points described above, and allocated data into values above (HI-EMG) or below (LOW-EMG) this mean to compare SAS and BIS agreement.

Descriptive data were analyzed using the mean value for continuous data and the median value for ordinal data. Dispersion was calculated using the standard deviation for continuous data and the interquartile range (IQR) for ordinal data. To assess the construct validity of SAS using a paired extreme-group approach [15], we hypothesized that SAS values would be lower at the time of ICU admission (Time 1) compared to post-extubation values (Time 4) using the Wilcoxon signed rank test. The BIS, VAS, EMG and other EEG-based variables were compared at these same times using paired *t*-tests. Spearman's rho was used to assess the correlation between SAS, VAS and the various EEG-based variables for all data obtained at the four time points identified a priori. Statistical significance required a p of less than 0.05. This study was conducted in accordance with the principles established in Helsinki and was approved by the institutional review board of Maine Medical Center.

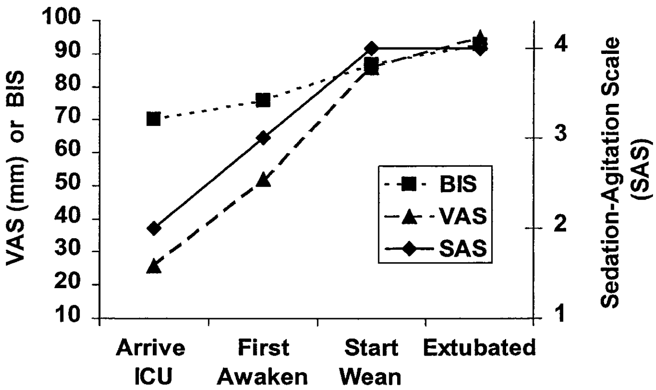

Fig. 2 Sedation-Agitation Scale (SAS), Bispectral Index (BIS) and Visual Analog Scale (VAS) measured at four times after cardiac surgery: upon arrival on the ICU, at first awakening, at the start of ventilator weaning and after extubation

Results

Thirty-nine patients were entered into this observational study upon arrival on the ICU after cardiac surgery. Male patients made up 69 % of the cohort ($n = 27$), the mean age was 66 ± 11 years and all patients survived to hospital discharge. The average bypass pump time was 97 ± 25 min, with a cross-clamp time of 65 ± 19 min. Anesthesia was administered using fentanyl ($n = 39$, mean dose 1041 ± 321 µg or 12.5 ± 5.4 µg/kg), midazolam ($n = 38$, mean dose 6.9 ± 3.3 mg), isoflurane ($n = 38$), pancuronium ($n = 36$, 13.3 ± 3.9 mg), sodium thiopental ($n = 10$, 302 ± 185 mg) and propofol ($n = 11$, 92 ± 68 mg). While being studied in the ICU, patients received sedation with midazolam (2.5 ± 1.8 mg) or propofol (initial infusion rate 18 ± 12 µg·kg·min) and analgesia with fentanyl (189 ± 83 µg) or morphine sulfate (13 ± 5 mg); one patient received both fentanyl and morphine sulfate.

Shortly after patients' arrivals in the ICU (Time 1), the median SAS score was 2 (IQR = 1–3), the mean VAS was 26 ± 30 mm and the mean BIS was 70 ± 16 (see Fig. 2). Two patients did not awaken during the 6-h monitoring period. For the remaining 37 patients reaching Time 2 (a mean of 55 min after Time 1), the median SAS was 3 (IQR = 3–3), the mean VAS was 52 ± 18 mm and the mean BIS 76 ± 15. For ten patients, the initial assessment in the ICU identified them to be awake already (i.e. Times 1 and 2 were synchronous); data from this single time were included for both the Time 1 and Time 2 descriptions, but were only included once during correlation testing. A trial of weaning from the ventilator was attempted in 24 patients during the 6-h study (Time 3 – a mean of 4.0 h after Time 1). The median SAS at Time 3 was 4 (IQR = 4–4), the mean VAS was 86 ± 12 mm and the mean BIS 87 ± 10. Fourteen patients were extubated within the 6-h window

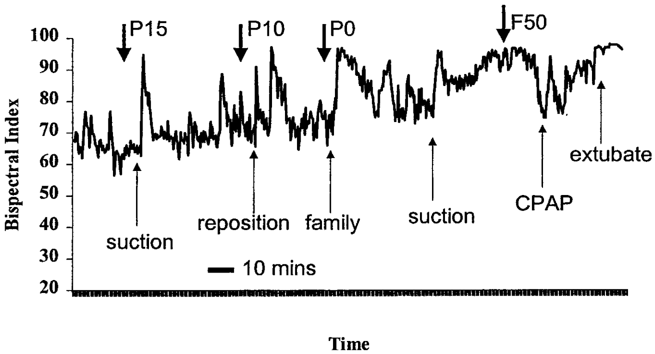

Fig. 3 Bispectral Index tracing of a 67-year-old woman after a two-vessel coronary bypass. Specific interventions such as suctioning, repositioning, family visit and liberation from the ventilator are identified under the BIS tracing. Reductions in her propofol infusion (to 15, 10 and 0 μg·kg·min) and bolus administration of fentanyl (50 μg) are identified above the BIS tracing. The BIS upon arrival on the ICU was 64 and at the time of extubation was 94

Table 2 Correlation between SAS and processed EEG variables

Parameters	r	p
SAS – BIS	0.61	< 0.001
SAS – median frequency	0.07	0.49
SAS – 95 % spectral edge	0.04	0.70
SAS – relative delta power	0.24	0.02
SAS – relative theta power	0.05	0.62
SAS – relative alpha power	0.29	0.005
SAS – relative beta power	0.038	0.72

with a median post-extubation SAS of 4 (IQR = 4–4), VAS of 95 ± 9 mm and BIS of 93 ± 9. Patients were not extubated within the 6-h period because of sedation (13), unstable hemodynamics (5), increased oxygen requirements (4), bleeding (2) or return to the operating room (1). Fig. 3 shows the BIS tracing of a 67-year-old woman after a two-vessel coronary artery bypass.

Using data from the four times identified a priori, SAS correlated well with VAS performed by one researcher ($r = 0.91$, $p < 0.001$) and VAS by 19 different bedside nurses ($r = 0.43$, $p < 0.001$). The BIS also correlated well with SAS ($r = 0.60$, $p < 0.001$) and with VAS performed by the single researcher ($r = 0.60$, $p < 0.001$). For the fourteen patients extubated during the 6-h study window, significant differences were observed between the time of ICU arrival (Time 1) and extubation (Time 4) for SAS [2 (1–3) versus 4 (4–4)], BIS (71 ± 13 versus 93 ± 10), VAS (32 ± 28 versus 95 ± 9 mm) and EMG (32 ± 8 versus 49 ± 7 dB), all $p < 0.001$. No significant differences were seen between these times for other EEG power spectral data. As shown in Table 2, SAS correlated well with BIS, less well with relative delta or alpha power, and did not correlate with other power spectral EEG parameters in this cohort.

For time points with EMG data available ($n = 94$), the mean EMG power was 39 dB, and the correlation between BIS and SAS was good ($r = 0.61$, $p < 0.001$), as was the correlation between BIS and VAS ($r = 0.62$, $p < 0.001$). Among patients with greater EMG power (HI-EMG), the BIS-SAS correlation was reduced ($r = 0.18$, $p = 0.20$, $n = 49$) compared to those with less EMG power (LOW-EMG, $r = 0.35$, $p = 0.018$, $n = 46$). The HI-EMG group was more awake as suggested by a higher value for SAS (4, IQR 4–4 versus LOW-EMG SAS of 3, IQR 1–3, $p < 0.001$), BIS (90 ± 9 versus 65 ± 13, $p < 0.001$) and VAS (78 ± 25 versus 35 ± 29 mm, $p < 0.001$). A small subset of very sedated patients exhibited an increased EMG signal, possibly a result of shivering or non-specific movements unassociated with wakefulness. This pattern of low SAS (1 or 2) or low VAS (< 30 mm) and high BIS (> 80) was seen in 2 of the 49 observations with above-average EMG activity (4 %).

Discussion

A validated and reliable scale to quantify sedation and agitation among adult ICU patients has been repeatedly called for during the last few years [1, 17]; this study confirms that SAS agrees well with other subjective and objective monitoring tools. Because no gold standard method to monitor sedation has been identified, construct validity was tested and confirmed, showing that BIS, SAS and VAS are lower upon arrival on the ICU than at the time of extubation after cardiac surgery. Additionally, SAS and BIS increase over time when measured in this cohort of patients awakening from anesthesia. These findings provide additional evidence that SAS is a valid and reliable scale with which to assess adult ICU patients [5, 6, 10, 11]. A very similar scale adapted from SAS has recently been shown to be valid and reliable [14, 18], and the reliability of SAS in the hands of ICU nurses not trained in its use was recently confirmed (weighted kappa > 0.85) [19].

The EEG spectral edge and median frequency values did not correlate with SAS or VAS in this ICU study and were not different when comparing values upon arrival in the ICU and following extubation, despite an obvious difference in the level of sedation as measured by SAS, VAS and BIS. The superiority of BIS in comparison to other EEG-based variables has been seen in several studies [20, 21]. Increasing drug doses are associated with a biphasic response of power spectrum-derived variables, initially inducing a faster EEG pattern, then slowing with additional drug administration. This complicates efforts to use frequency-based variables such as the 95 % spectral edge or median frequency, and may explain the lack of a difference in these variables between Times 1 and 4 [8, 22].

The higher values for SAS, BIS and VAS among the HI-EMG group are not surprising since awake patients would be expected to move more (with an associated increased power in the EMG frequency range). The decreased correlation between SAS and BIS associated with separating patients based on the EMG signal suggests that the EMG may affect the accuracy of the BIS, but reductions in sample size and value range may also have contributed to the decreased correlation. Though associated with increased wakefulness, increased EMG power was also seen among some sedated patients. Among patients not receiving neuromuscular blockade, EMG may artifactually increase the BIS, suggesting to clinicians that the patient is more awake than is true. This low SAS or VAS and high BIS pattern was uncommon in our select cohort of patients, occurring in only 4 % of the patients. Differentiating between EMG data that identifies increased wakefulness and non-specific muscle activity in more sedated patients is a difficult challenge that has been previously recognized [23, 24]. The BIS monitors measure and display indices of signal quality and EMG power, which may allow users to identify this potential problem.

Our study was designed to validate SAS after cardiac surgery and used a model in which patients arrive in the ICU still anesthetized from their surgery and awaken over the next few hours. Although similar models have been used to evaluate other "sedation" scales, our conclusions may not be applicable to all ICU patients and only addressed the range of sedation or wakefulness attained by patients as they awakened after cardiac surgery. Other reports have previously assessed a broader spectrum of agitation and sedation with the SAS [6] and deeper levels of sedation with the BIS [25, 26].

Not all patients were extubated during the study period or attained all four time points identified a priori; the construct validation in our study was based on the 14 patients who were extubated. Following patients for longer than 6 h after arrival in the ICU would have increased the number of patients proceeding to extubation and provided a larger sample. Despite the statistical differences noted for the BIS, SAS and VAS between Times 1 and 4, it is possible that this study was underpowered to detect differences in the other power spectral variables. A significant number of patients were not extubated during the study, due to delayed awakening from anesthesia or possibly from sedation administered in the ICU. It is possible that using a scale such as the SAS or BIS to guide postoperative sedation may reduce oversedation, but we did not design our study to test this important hypothesis. Our method to calculate BIS values in the ICU is an initial effort in that regard and future studies should confirm that this approach is effective or improve upon it.

The SAS appears to be a valid measure of wakefulness for ICU patients after cardiac surgery, as supported by the strong correlation with independent subjective (VAS) and objective (BIS) assessments of sedation and the differences noted between ICU arrival and extubation. Although a significant correlation exists between subjective scores and the BIS, the EMG signal may elevate the BIS value for a small number of sedated patients and remains a potential artifact among ICU patients not receiving neuromuscular blockade. Future revisions of the BIS algorithm to address this EMG problem or incorporating the signal quality and EMG power detectors inherent in the BIS monitors may also prove useful.

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