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Effects of Bispectral Index Monitoring on Recovery from Surgical Anesthesia in 1,580 Inpatients from an Academic Medical Center

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Background: **The purpose of this study was to determine whether monitoring Bispectral Index (BIS) would affect recovery parameters in patients undergoing inpatient surgery.**

Methods: **Anesthesia providers (n = 69) were randomly assigned to one of two groups, a BIS or non-BIS control group. A randomized crossover design was used, with reassignment at monthly intervals for 7 months. Duration of time in the postanesthesia care unit, time from the end of surgery to leaving the operating room, and incidence of delayed recovery (> 50 min in recovery) were compared in patients treated intraoperatively with or without BIS monitoring. Data were analyzed by analysis of variance, unpaired *t* test, or chi-square test as appropriate.**

Results: **One thousand five hundred eighty patients in an academic medical center were studied. The mean BIS in the monitored group was 47. No differences were found in recovery parameters between the BIS-monitored group and the control group when comparisons were made using all subjects or when data were analyzed within anesthetic subgroups stratified by anesthetic agent or duration of anesthesia. There were some small reductions in the intraoperative concentration of sevoflurane (but not isoflurane).**

Conclusions: **The use of BIS monitoring for inpatients undergoing a wide variety of surgical procedures in an academic medical center had some minor effects on intraoperative anesthetic use but had no impact on recovery parameters.**

IT has been postulated[1,2] that the Bispectral Index (BIS) may be used to titrate volatile anesthetics more precisely to individual anesthetic requirements than would otherwise be possible by usual clinical methods. This may potentially avoid exposure to unnecessarily high concentrations of anesthetics while at the same time minimizing the likelihood of awareness during anesthesia. Such benefits, if they exist, might be expected to correlate with faster emergence, faster turnover between cases, shorter recovery times in the postanesthesia care unit (PACU), and decreased adverse effects of anesthesia (drowsiness, postoperative nausea and vomiting,[3] and shivering).

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In a previously reported study of 585 patients undergoing ambulatory surgery,[4] we observed a 13% reduction in mean end-tidal sevoflurane concentration in both sexes and an 11% reduction in the recovery time (time to discharge) in male patients when the BIS was used to monitor anesthetic depth. There are a number of other studies, mostly in outpatients, that also show a reduction in anesthetic dose and improvements in various measures of recovery when the BIS was used as an aid to titrating anesthetics.[1,2,5–10]

The purpose of the current study was to determine whether the introduction of mandatory BIS monitoring throughout an entire operating complex of an academic medical center would influence the recovery process of inpatients undergoing a variety of surgical procedures. In these patients, who required at least overnight hospitalization, we expected greater heterogeneity of anesthetic techniques and duration of surgery as compared with outpatient surgery, both of which might alter the utility of BIS monitoring in expediting recovery after surgery.

We tested the hypothesis that BIS monitoring would result in a shorter recovery period both in the operating room during emergence and in the PACU. We also hypothesized that BIS monitoring would be associated with use of lesser concentrations of potent volatile anesthetics and possibly reduced anesthesia-related adverse effects. The primary endpoints of the study were total time spent recovering in the PACU and mean end-tidal concentration of potent inhaled anesthetics. As secondary endpoints, we determined the time from the end of surgery to exit from the operating room, as one aspect of anesthesia-controlled turnover time, and the time to achieve an Aldrete score of 9–10, as a general indication of the speed of arousal. We also ascertained the incidence of delayed discharge from the PACU and the reasons attributed to such delays to determine whether qualitative differences in the recovery process might exist between BIS-monitored and control groups.

Materials and Methods

The study was approved by the Institutional Review Board at the University of Washington (Seattle, Washington) as a prospective comparison of outcomes of patients anesthetized by personnel who were randomly assigned to provide anesthesia with or without the use of BIS monitoring. The methods used are similar to those

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reported previously.[4] BIS® monitors (model A-1050 EEG monitor; Aspect Medical Systems, Natick, MA) were installed in all of the 18 operating rooms of a university teaching hospital. There was an initial introductory period of 3 months to allow anesthesia providers (anesthesia attending staff, residents, and nurse anesthetists) to become familiar with the use of the BIS® monitor. The primary anesthesia providers were 18 certified registered nurse anesthetists and 51 residents in training—19 in clinical anesthesia year 1, 16 in clinical anesthesia year 2, and 17 in clinical anesthesia year 3. They were supervised by 41 different anesthesia attending faculty members. The study was performed over a 7-month period and included all patients undergoing general anesthesia who were scheduled to stay in the hospital postoperatively. Patients having head and neck surgery or surgery in the prone position were excluded to avoid possible difficulty in securing a BIS® sensor. We also excluded patients scheduled to recover in an intensive care unit, because the recovery process of these patients is different from recovery in the PACU.

All anesthesia providers were given written and verbal information regarding the use and the significance of the BIS before beginning the study. They were told that (1) a suggested target level for the BIS is 50–60, (2) a BIS of less than 70 is adequate to prevent conscious recall, (3) movement may occur at a BIS of less than 70, and (4) patient safety should be the first priority. They were also advised that movement would be less likely if patients were given adequate analgesia.[11] The type of anesthetic to be administered was left to the discretion of the anesthesia provider. BIS® electrodes were applied before surgery on patients in the BIS group and were removed before the patient left the operating room.

Anesthesia providers were randomly assigned to a BIS or control group for the first month, at the end of which they were reassigned using a crossover design to the alternate group. At the end of the second month, all participants were again randomly assigned to a BIS or control group, followed by crossover at 1-month intervals for nonrotating personnel (certified registered nurse anesthetists and faculty). Residents, who rotated into the institution from other hospitals where BIS monitoring was not available, received equivalent training and random group assignment with crossover at monthly intervals. Patients were excluded from the study if the anesthesia provider did not adhere to the randomization scheme. There was no financial or other type of inducement for the anesthesia providers to participate in the study.

The anesthesia providers recorded patient demographic characteristics and details of the anesthetic on separate data collection forms. The primary outcome variable was duration of stay in the PACU. This was determined as the time from the patient's arrival in the PACU to the time the patient was discharged to the ward. We defined recovery as delayed when patients remained in the PACU for more than 50 min.[4] When this occurred, the nurse caring for the patient indicated the reasons for delay using a preprinted list of causes, which included medical, surgical, and system factors. Only the three most important factors were recorded. As secondary endpoints, we recorded the time from the end of surgery to when the patient exited the operating room and the time for the patient to achieve an Aldrete score of 9–10. The end-tidal anesthetic gas concentrations and BIS values were recorded manually every 15 min during the case. The mean end-tidal anesthetic concentration was calculated for each patient as the average of all concentrations, excluding the first and last measurements. A dedicated nurse, specialized in quality assurance, reviewed all anesthesia records on a daily basis and verified the accuracy of data provided and compliance with the randomization scheme. An employee specifically assigned to the project then entered the data into a computer database.

Statistical Analysis

The sample size was based on a previous study in which we observed a mean recovery time (± SD) of 164 ± 59 min in women and 151 ± 40 min in men undergoing general isoflurane anesthesia for outpatient surgery.[12] By using the previous data to calculate standardized differences, a power analysis predicted a required sample size of approximately 120 women or 55 men for 80% power to detect a 30-min difference, with an α of 0.05 for 500 women and 250 men to detect a 15-min difference. We assumed a 15-min difference was the smallest difference that would be of clinical relevance and therefore predicted that we would require approximately 750 patients. We also assumed that further subgroup analysis might be required to adequately test our hypotheses and therefore predicted that up to 1,500 patients might be required for the study. We predicted that 6 months of data collection would be required and therefore collected data for 1 additional month to ensure an adequate sample size.

Means and SEs were calculated for continuous data. Comparisons between groups were by unpaired *t* tests for two groups or analysis of variance for more than two groups with *post hoc* comparisons by Bonferroni–Dunn. Comparison of proportions was made by the chi-square test. Linear correlation analysis was performed to identify significant associations between variables and linear regression analysis used to determine the potential contribution of independent variables to outcomes. An overall *P* value of 0.05 was considered significant.

Results

A total of 1,698 patients initially met the criteria for study. A preliminary analysis revealed that 1,580 (93%)

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received thiopental or propofol for induction, with isoflurane or sevoflurane for maintenance of anesthesia. The major analyses of data were therefore performed on this restricted, relatively homogeneous set of cases. Because a preliminary analysis also indicated there were significant correlations between recovery time and the duration as well as the type of anesthetic, we chose to evaluate the effect of BIS in retrospectively stratified anesthetic subgroups (based on anesthetic type and anesthetic duration) as well as in the whole group of 1,580 patients. The anesthetic subgroups included thiopental–isoflurane, propofol–isoflurane, thiopental–sevoflurane, and propofol–sevoflurane for induction and maintenance, respectively. The anesthesia duration categories were as follows: 0–100, 101–200, 201–400, and longer than 400 min.

Overall, the mean (± SE) time-averaged BIS value at which the 1,698 patients were maintained (excluding first and last measurements) was 47 ± 0.25 (median, 47). The mean BIS at 15 min from the end of surgery was 53 ± 0.47, and the mean BIS at the end of surgery was 65 ± 0.69. There were no differences in recovery parameters between BIS and control groups when all patients (1698) were considered without regard to anesthetic type or duration. PACU times were 94 ± 1.6 *versus* 92 ± 1.3 min for BIS and control groups, respectively ($P = 0.35$). Times from the end of surgery to leaving the operating room were 9.7 ± 0.17 *versus* 9.7 ± 0.17 min ($P = 0.99$), and times to reach an Aldrete score of 9–10 were 16.8 ± 1.3 *versus* 14.8 ± 0.9 min, respectively ($P = 0.2$).

The demographic characteristics and details of anesthesia in the major subset of 1,580 patients who constituted the sample for all subsequent analyses are presented in table 1. There were no demographic differences between the BIS-monitored and control patients and no differences in the distribution of surgical procedures separated into groups as follows: abdominal surgery (38%), minor orthopedics (24%), minor body surface surgery (20%), major orthopedics (11%), and major body surface surgery (6%). There was also no significant difference between BIS and controls in the frequency of use of various opioid drugs (fentanyl, alfentanil, remifentanil, morphine); patients in the BIS-monitored group received slightly less fentanyl in $\mu g \cdot kg^{-1} \cdot min^{-1}$. The percentage of patients paralyzed for intubation (75 *vs.* 78% in BIS and control groups, respectively), the percent of patients in whom neuromuscular blockade was maintained after intubation (44 *vs.* 42% in BIS and control groups, respectively), and the distribution of the type of neuromuscular blocker used were also not different in BIS and control groups (not shown in the table).

Data relating to the duration of PACU stay are shown in figure 1, and statistical comparisons in table 2. Overall, BIS monitoring made no difference to the mean duration of PACU stay, either within the entire population of 1,580 patients, or within individual subgroups. There was also no effect of BIS monitoring on the time in PACU to achieve an Aldrete score of 9–10 (table 2) or the time to exit the operating room after the completion of surgery (9.6 ± 0.18 and 9.6 ± 0.17 min in BIS and control groups, respectively).

Table 1. Demographic Characteristics and Anesthetic Drugs in the Study Population

Variable	BIS	Control
Number of patients	749	831
Mean BIS	47 (0.25)	—
Number female (%)	420 (56)	449 (54)
Age, yr	46 (0.6)	47 (0.8)
Weight, kg	80 (0.8)	79 (0.8)
Type of surgery		
Abdominal	296 (40)	305 (37)
Minor orthopedic	196 (26)	176 (21)
Major orthopedic	73 (10)	106 (13)
Minor body surface	135 (18)	171 (21)
Major body surface	37 (5)	57 (7)
NA	31 (0.4)	9 (1)
Duration of surgery, min	146 (3)	147 (3)
Duration anesthesia, min	173 (3)	173 (3)
Duration of anesthesia stratified by time, n (%)		
0–100 min	157 (21)	200 (24)
101–200 min	342 (46)	338 (41)
201–400 min	231 (31)	275 (33)
> 400 min	17 (2)	15 (2)
ASA physical status		
I	201 (27)	218 (26)
II	405 (54)	452 (54)
III	142 (19)	159 (19)
IV	1 (0.13)	2 (0.24)
Thiopental–isoflurane	246 (35)	291 (35)
Thiopental–sevoflurane	95 (13)	112 (13)
Propofol–isoflurane	124 (17)	142 (17)
Propofol–sevoflurane	284 (38)	286 (34)
N_2O used	582 (78)	656 (79)
Fentanyl used	665 (89)	730 (88)
Fentanyl, $\mu g \cdot kg^{-1} \cdot min^{-1}$	0.023*	0.025
Alfentanil used	1 (0.1)	0
Remifentanil used	13 (1.7)	16 (1.9)
No opioids	37 (5)	44 (5)
Regional block + general anesthesia	159 (21)	166 (20)
Number intubated (%)	584 (78)	676 (81)

Values are mean (SE) or n (%).

* $P < 0.001$ for Bispectral Index (BIS) *vs.* control.

ASA = American Society of Anesthesiologists; NA = other surgical procedures; N_2O = nitrous oxide.

Although there were no differences detected between BIS and control groups, we did observe significant differences in PACU duration related to the type and duration of anesthesia (table 2 and fig. 2). Thiopental induction was associated with a 16-min-longer recovery period compared with propofol (101 *vs.* 85 min; $P < 0.0002$), and isoflurane maintenance was associated with a 19-min-longer recovery period (102 *vs.* 83 min; $P < 0.0001$) compared with sevoflurane. These differences were most evident in cases longer than 200 min in duration. When divided into four subgroups on the basis of induc-

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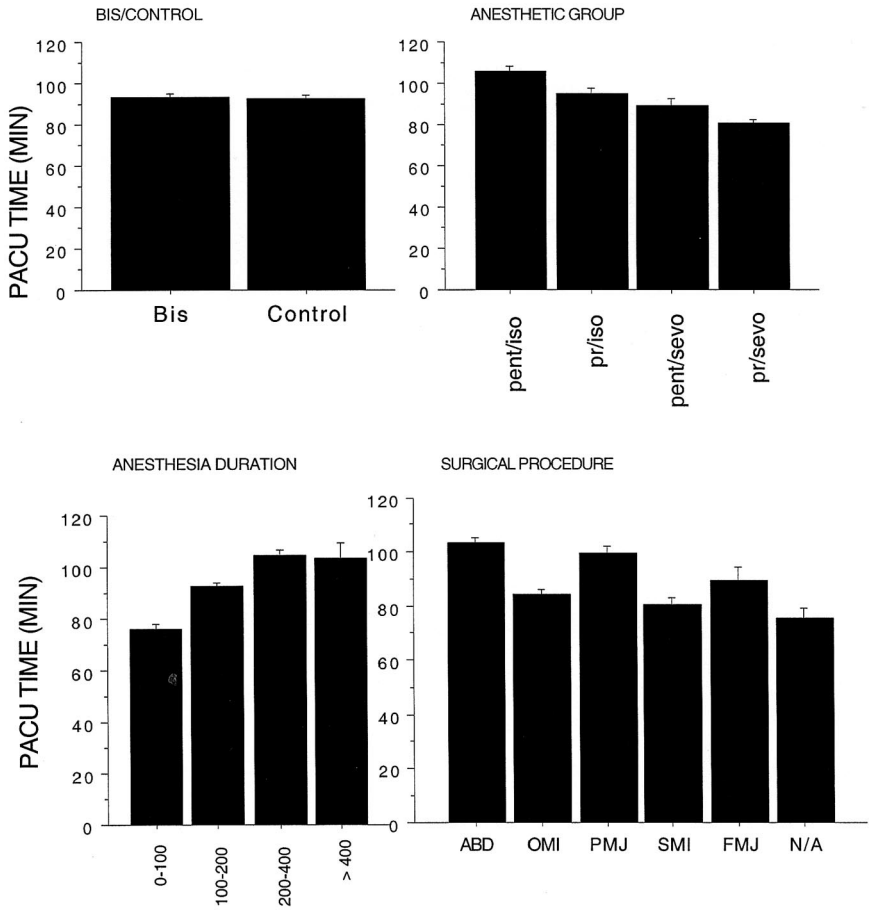

Fig. 1. Comparisons of total time in the postanesthesia care unit (PACU) in different clinical categories. (*Upper left*) Comparison of Bispectral Index (BIS)–monitored patients and controls. (*Upper right*) Comparison by anesthetic groups: pent/iso = thiopental–isoflurane; pr/iso = propofol–isoflurane; pent/sevo = thiopental–sevoflurane; pr/sevo = propofol–sevoflurane. $P < 0.0001$ by analysis of variance for all groups. P values for intergroup comparisons: pr/sevo *versus* pent/sevo, $P = 0.0169$; pent/iso *versus* pr/iso, $P = 0.0003$; pr/sevo *versus* pr/iso, $P < 0.0001$; pent/iso *versus* pent/sevo, $P < 0.0001$; pr/sevo *versus* pent/iso, $P < 0.0001$; pr/iso *versus* pent/sevo, P = not significant. (*Lower left*) Comparison of groups categorized by duration of anesthesia: $P < 0.0001$ by analysis of variance. For all groups, P values for intergroup comparisons: 0–100 *versus* 101–200 min, $P < 0.0001$; 101–200 *versus* 201–400 min, $P < 0.0001$. (*Lower right*) Comparisons of surgical categories. ABD = abdominal surgery; FMJ = major body surface surgery; N/A = other surgical procedures; OMI = minor orthopedic surgery; PMJ = major orthopedic surgery, SMI = minor body surface surgery. $P < 0.0001$ by analysis of variance for all groups.

tion and maintenance agents, recovery was longest in the thiopental–isoflurane group and shortest in the propofol–sevoflurane group (a difference of 25 min: 106 *vs.* 81 min; $P < 0.0001$). There were similarly significant differences between anesthetic subgroups in the time to achieve an Aldrete score of 9–10 and to exit the operating room at the end of surgery, although the absolute differences were of much smaller magnitude.

When we compared the end-tidal gas concentrations of isoflurane or sevoflurane in relation to BIS monitoring and anesthetic group (table 3), we observed a statistically significant but small reduction in end-tidal sevoflurane concentration (4.7%, $P = 0.046$) and a trend, albeit not significant, toward a reduction in isoflurane concentration (2.7%) associated with the use of the BIS. If the analysis included only cases in which nitrous oxide was not used, the differences were greater (−9.4% for sevoflurane, $P = 0.06$; −7.5% for isoflurane, $P = 0.07$) and approached significance, but the power of the analysis was reduced because of the smaller number of cases included in the analysis.

The incidence of delayed discharge is shown in table 4. Overall, we observed no effect of BIS monitoring on the incidence of delayed discharge. In table 5, the factors identified as being causally related to delayed discharge (> 50 min in the PACU) are shown in relation to BIS monitoring. A variety of factors contributed to delayed discharge from the PACU. The most common medical causes were postoperative pain followed by drowsiness, and postoperative nausea and vomiting. In the patients who received pentothal for induction with isoflurane for maintenance, drowsiness was less often reported as a cause of delayed discharge in the BIS-monitored group (34% in the BIS group *vs.* 47% in controls; $P < 0.01$). Nausea, however, was more frequent in the same subgroup (21% in the BIS group *vs.* 13% in controls; $P = 0.03$). There were no other significant differences between BIS and controls in the frequency of pain, drowsiness, nausea, or shivering as causes of delayed discharge.

To assess whether any learning effect occurred over the course of the study, we performed correlation analyses between the date of surgery and outcome parameters of interest (PACU duration, end of surgery to exit from the operating room, and time in recovery to achieve an Aldrete score of 9–10). There were no significant relations detected by linear correlation analysis (r values 0.0003–0.024; P values 0.29–0.99).

Discussion

Two recent studies have indicated that monitoring the BIS reduces the incidence of awareness during anesthe-

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Table 2. PACU Duration and Time to Attain an Aldrete Score of 9–10 in Patients Stratified by Anesthetic Group, and Duration of Anesthesia

	PACU Duration, min (SE)				Time to Aldrete score 9–10, min (SE)			
	BIS	Control	BIS *vs.* Control*	All Patients	BIS	Control	BIS *vs.* Control*	All Patients
All patients (n = 1,580)	93 (1.7)	92 (1.4)			16.8 (1.3)	14.8 (0.9)	NS	
Individual anesthetic agents (n = 1,580)								
Thiopental (n = 744)	104 (3)	100 (2)	NS	101 (1.6)	21.5 (2.3)	20.4 (1.8)	NS	20.9 (1.4)
Propofol (n = 835)	85 (2)	86 (2)	NS	85 (1.3)	12.6 (1.3)	10.2 (1)	NS	11.4 (1.6)
Interagent comparison*				$P < 0.0002$				$P < 0.0001$
Isoflurane (n = 803)	104 (2)	100 (2)	NS	102 (1.5)	21.3 (2.1)	19.7 (1.5)	NS	20.4 (1.3)
Sevoflurane (n = 777)	82 (2)	84 (2)	NS	83 (1.4)	11.8 (1.4)	10.1 (1)	NS	10.9 (0.9)
Interagent comparison*				$P < 0.0001$				$P < 0.0001$
Anesthetic groups								
Thiopental–isoflurane (n = 537)	108 (3)	104 (2)	NS	106 (1.9)	21.9 (1.7)	23.6 (2)	NS	22.8 (1.6)
Thiopental–sevoflurane (n = 207)	91 (6)	87 (4)	NS	89 (3.2)	20.3 (1.5)	12.5 (1.8)	NS	15.8 (2.3)
Propofol–isoflurane (n = 266)	97 (4)	93 (3)	NS	95 (2.4)	20.3 (1.4)	12.1 (1.7)	NS	15.9 (1.8)
Propofol–sevoflurane (n = 570)	79 (2)	82 (2)	NS	81 (1.5)	9.4 (1.2)	9.2 (1.2)	NS	9.3 (0.8)
Interagent comparisons*				$P < 0.0001$				NS
Anesthetic duration, min								
0–100 (n = 357)	73 (3)	78 (2)	NS	77 (2)	10.2 (1.3)	10.9 (1.3)	NS	10.4 (0.9)
101–200 (n = 680)	100 (2)	97 (2)	NS	98 (2)	19.4 (2.0)	15.6 (1.5)	NS	17.6 (1.3)
201–400 (n = 506)	104 (4)	102 (3)	NS	105 (2)	18.6 (2.5)	20 (2.1)	NS	19.4 (1.6)
> 400 (n = 32)	99 (13)	102 (17)	NS	100 (10)	21.7 (12.8)	23.5 (4.3)	NS	22.6 (9.5)
Intergroup comparison*				$P < 0.0001$				$P < 0.0001$

* Bispectral Index (BIS) *vs.* control by unpaired *t* test; other intergroup comparisons by analysis of variance. Values are mean (SE).

NS = not significant; PACU = postanesthesia care unit.

sia.[13,14] It has also been suggested by numerous investigators, mostly in outpatients, that BIS monitoring may be used to titrate anesthetic depth, reduce exposure to anesthetic agents, and thus hasten recovery and discharge from the PACU.[1,2,5–10] In the current study, we failed to demonstrate any impact of BIS monitoring on recovery parameters in a large, diverse group of patients undergoing inpatient surgery in an academic medical center. In particular, we were unable to demonstrate a reduction in duration of time patients spent in the operating room at termination of surgery or subsequently in the PACU before discharge to the ward.

Our results differ from those of Johansen *et al.*,[10] who, in a similar inpatient study, reported shorter times to emergence (4 min), to exit from the operating room (3 min), and to discharge from the PACU (15 min) when BIS monitoring was used to monitor depth of anesthesia. However, Johansen *et al.* used a retrospectively selected subgroup of patients in whom the BIS was successfully maintained between 50 and 65 for a least 34% of the case, to compare to the unmonitored control group. In our study, the average BIS value was 47, lower than that of the BIS subgroup selected for study by Johansen *et al.* The results reported in our study may be more representative of the range of outcomes that can be anticipated with anesthesia provided by a wide spectrum of anesthesia providers in a teaching hospital. Although this may more closely approach the real-life situation than one artificially manipulated for the purpose of research, additional variability may have been introduced by being conducted in a teaching institution.

Other smaller studies have investigated the effects of BIS monitoring on emergence and recovery in the inpatient setting. One such study of elderly patients undergoing joint replacement reported faster times to orientation and to achieve an Aldrete score greater than 9 in the PACU when BIS monitoring was used to titrate the depth of isoflurane anesthesia,[8] but no significant effect on time to discharge from the PACU was observed. Investigations of BIS monitoring on recovery parameters in ambulatory surgery have shown variable results. Pavlin *et al.*[4] reported an 11% (19-min) faster recovery and discharge in male but not female ambulatory patients when BIS monitoring was used to titrate sevoflurane There are also reports of more rapid emergence after propofol infusion using BIS monitoring but not after

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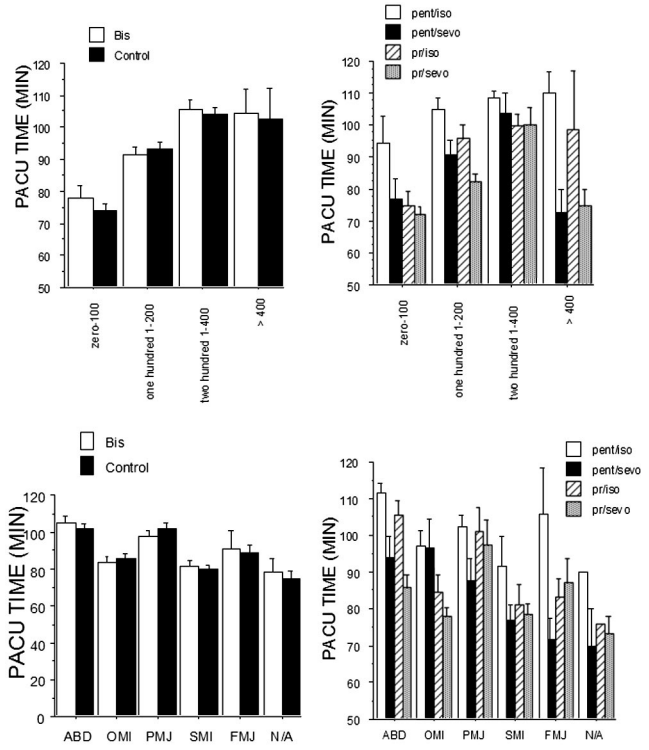

Fig. 2. Interactions of Bispectral Index (BIS) monitoring, anesthetic duration, surgical procedure, and anesthetic technique on time spent in the postanesthesia care unit (PACU). (*Upper left*) Comparison of PACU duration in BIS-monitored patients and controls separated into categories based on anesthetic duration (0–100, 101–200, 201–400, > 400 min). Not significant for BIS-monitored patients *versus* controls. (*Upper right*) Comparison of PACU duration in four anesthetic groups, separated into categories based on anesthetic duration (0–100, 101–200, 201–400, > 400 min). $P < 0.05$ by analysis of variance for 0–100, 100–200, and longer than 400 min. (*Lower left*) Comparison of PACU duration in BIS-monitored patients and controls separated into categories based on surgical procedure. ABD = abdominal surgery; FMJ = major body surface surgery; N/A = other surgical procedures; OMI = minor orthopedic surgery; PMJ = major orthopedic surgery, SMI = minor body surface surgery. Not significant for BIS-monitored patients *versus* controls. (*Lower right*) Comparison of PACU duration in four anesthetic groups separated into categories based on surgical procedure.

sevoflurane[7] or desflurane.[6] Song *et al.*,[1] using volatile agents, and Gan *et al.*,[5] using propofol and alfentanil infusions, both demonstrated significantly more rapid emergence but no difference in PACU discharge times when BIS monitoring was used to titrate anesthetic depth between 45 and 60. A recent study found that BIS monitoring had no impact on the ability to fast-track patients after out patient gynecologic laparoscopy.[15]

In our study, we observed only a small reduction (4.7%) in the average end-tidal concentration of sevoflurane used to maintain anesthesia in the BIS-monitored group and an insignificant difference in the average concentration of isoflurane. Therefore, it is not surprising that we did not detect differences in speed of recovery. Other studies, however, have reported significant reductions in anesthetic use and end-tidal gas concentrations when the anesthetic was titrated within a particular BIS range.[5,6,8,9] In one study by Song *et al.*,[1] a mean BIS of 50–60 was reported in 60 patients who were anesthetized with either sevoflurane or desflurane and paralyzed with mivacurium throughout the duration of surgery. Significantly less desflurane and sevoflurane were used in the BIS-monitored groups (end-tidal desflurane 4.2% *vs.* 2.3% and end-tidal sevoflurane 1.8% *vs.* 0.9%, respectively, in non-BIS controls and BIS groups). In that study, 23% of the BIS-monitored patients were reported as coughing and bucking compared with 10% of patients in

Table 4. Role of BIS and Other Factors in Determining the Incidence of Delayed Discharge from PACU*

Grouping variable	Group	% Delayed	*P* Value (Chi-square)
BIS use	BIS	92	NS
	Control	92	
Nitrous oxide	N_2O	91.3	NS
	No N_2O	93.3	
Inhaled anesthetic	Isoflurane	95.5	< 0.0001
	Sevoflurane	88.0	
Induction agent	Thiopental	95.3	< 0.0001
	Propofol	88.7	
Anesthetic group	Thiopental–isoflurane	96.8	< 0.0001
	Thiopental–sevoflurane	91.3	
	Propofol–isoflurane	92.9	
	Propofol–sevoflurane	86.8	
Duration of anesthesia	0–100	82.6	< 0.0001
	101–200	91.3	
	201–400	98.6	
	> 400	96.9	

* Defined as > 50 min in postanesthesia care unit (PACU).

BIS = Bispectral Index; N_2O = nitrous oxide; NS = not significant.

Table 3. Mean End-tidal Gas Concentrations with and without BIS Monitoring

Anesthetic Agent	End-tidal Gas Concentrations, %			
	BIS	Control	% Change	*P* Value
All sevoflurane (n = 766)	1.21 (0.02)	1.27 (0.02)	−4.7	0.046
Sevoflurane without N_2O (n = 133)	1.35 (0.05)	1.45 (0.06)	−9.4	0.06
Sevoflurane with N_2O (n = 633)	1.18 (0.02)	1.22 (0.02)	−0.3	0.16
All isoflurane (n = 625)	0.74 (0.02)	0.76 (0.02)	−2.7	0.43
Isoflurane without N_2O (n = 162)	0.86 (0.03)	0.93 (0.03)	−7.5	0.07
Isoflurane with N_2O (n = 463)	0.70 (0.03)	0.71 (0.02)	−1.4	0.86

Values are mean end-tidal concentration in percent (SE), or percent change.

BIS = Bispectral Index; N_2O = nitrous oxide.

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Table 5. Factors Reported as Causing Delays in PACU Discharge

	BIS	Control
System and medical, n (%)	93 (16)	97 (15)
System only, n (%)	41 (7)	51 (8)
Medical only, n (%)	382 (66)	410 (65)
No delay, n (%)	61 (11)	69 (11)
Medical causes, n (%)		
Pain, n (%)	308 (60)	320 (57)
Drowsiness, n (%)	151 (29)	186 (33)
Nausea/vomiting, n (%)	101 (20)	93 (17)

There are no significant differences between Bispectral Index (BIS) and control values.

PACU = postanesthesia care unit.

the non-BIS group. However, there was no statistical testing offered to show a difference in the incidence of airway irritation between the groups. In our study, the mean BIS was 47, lower than in some other studies.[1,5,7] In addition, the mean end-tidal sevoflurane concentration in our control group that received sevoflurane without nitrous oxide was 1.49%. Because the maintenance concentrations were lower in our patients than in the control group in the study by Song *et al.*,[1] it is perhaps not surprising that BIS monitoring had less effect in our patients than in the latter study.

Our study may be criticized because we did not include concealed BIS monitoring in our control group (*i.e.*, invisible to the anesthesia providers), a study design used by some investigators. The design of our study did not allow for such monitoring in the control group. In studies that have used concealed BIS monitoring in the control group, the BIS values were always higher in the group with visible BIS monitoring.[1,5–7,9] Therefore, there has been a general tendency toward lighter planes of anesthesia when the BIS is visible. The failure in our study to maintain patients at BIS values above 50 and reduce anesthetic concentration to a greater degree may have occurred for several reasons: surgical procedures that were generally more complex than outpatient surgery, lack of motivation of anesthesia providers to reduce the depth of anesthesia in patients who are known to be staying at least overnight, concerns that the patients may move in response to surgical stimulation, and lack of understanding of the application of BIS technology. It is also possible that the there was a learning process associated with use of the BIS that was ongoing during the conduct of the study in both groups and caused an overall improvement in the ability to accurately titrate anesthetic to requirements which persisted even when not using the BIS® monitor. However, there was no difference in mean BIS measurements or PACU duration over the course of the study arguing against such a hypothesis. Conceivably, a learning process could have occurred during the preliminary introductory phase, before starting the study.

In animals, recovery from anesthesia has been demonstrated to be inversely related to anesthetic exposure (both duration and dose).[16] However, the assumption that using the BIS to titrate anesthetic depth in patients will result in decreased anesthetic delivery and thereby hasten recovery is probably an oversimplified model, particularly in patients undergoing more complex inpatient surgical procedures. In fact, the duration of time patients stay in a recovery unit in some instances is mostly a reflection of system factors[12] (*e.g.*, how busy the nurses are, availability of orderlies for transport of patients to the ward) as demonstrated by our data (table 3). However, because we were able to detect significant differences in the recovery times related to anesthetic agents and to duration of surgery suggests that it would have been possible to alter recovery times by varying the intraoperative management of patients if the magnitude of an effect was clinically great enough to be relevant. However, given the multiplicity of medical and nonmedical factors that contribute to discharge delays,[17] the ability to alter recovery time by small adjustments in delivered anesthetic concentration may be an unrealistic expectation, particularly when using anesthetics of low solubility, such as sevoflurane, for inpatient surgery.

Overall, our study and other data in the literature suggest that BIS monitoring may be most efficacious in altering anesthetic utilization and recovery processes when used in an outpatient setting where motivation to expedite recovery is high. It may also be more effective when used by a small, homogeneous group of anesthesia providers who are comfortable with and dedicated to the concept of titrating anesthesia in the interests of promoting rapid recovery. It is also possible that it might play a more significant role in regulating anesthetic depth when using total intravenous anesthesia where there is no online feedback regarding plasma drug concentrations.

In our study, we did observe differences in recovery times related to duration of anesthesia and the choice of anesthetics. When compared separately or in combination, propofol and sevoflurane produced significantly shorter recovery times than thiopental and isoflurane for cases lasting less than 200 min (up to 25 min for propofol–sevoflurane *vs.* thiopental–isoflurane). Because this study was not specifically designed to compare the effects of anesthetic drugs, it is possible that the differences in recovery times could have been the result of bias in the selection of anesthetic drugs by the anesthesia providers. Therefore, isoflurane and thiopental may have been selected when there was no desire to promote rapid recovery. However, the differences between anesthetic groups persisted regardless of the type or duration of surgery and whether BIS monitoring was used, suggesting that expedited recovery was at least in part related to the pharmacologic properties of the anesthetics used. The collective effects of a difference of the

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magnitude observed in this study, when applied to all patients presenting for surgery, could have considerable impact on recovery room resources. Further investigation of a large, prospective, randomized group would be required to establish whether these findings are valid under controlled circumstances.

In summary, introduction of mandatory BIS monitoring for patients undergoing a wide variety of inpatient surgical procedures in an academic medical center resulted in a mean BIS of 47. BIS monitoring in this context did not reduce the duration of acute recovery in PACU and had minimal effect on the concentrations of potent inhaled anesthetics used to maintain anesthesia.

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