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BIS Monitoring to Prevent Awareness during General Anesthesia

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Background: **Unexpected awareness is a rare but well-described complication of general anesthesia that has received increased scientific and media attention in the past few years. Transformed electroencephalogram monitors, such as the Bispectral Index monitor, have been advocated as tools to prevent unexpected recall.**

Methods: **The authors conducted a power analysis to estimate how many patients would be needed in an appropriately powered study to demonstrate the Bispectral Index monitor reduces awareness, as well as a cost analysis to assess the cost of using the monitor for this purpose alone.**

Results: **If unexpected recall is rare (1 in 20,000), it will require a large study to demonstrate that the monitor reduces awareness (200,000–800,000 patients), and the cost of using it for this purpose alone would be high ($400,000 per case prevented). If awareness is common (1 in 100), then the number of patients needed in a study to demonstrate that the monitor works becomes tractable (1,000–4,000 patients), and the cost of using the monitor for this purpose alone becomes lower ($2,000 per case prevented). Because there are reported cases of awareness despite Bispectral Index monitoring, the authors are certain that the effectiveness of the monitor is less than 100%. As the performance of the monitor decreases from 100%, the size of the study needed to demonstrate that it works increases, as does the cost of using it to prevent awareness.**

Conclusion: **The contention that Bispectral Index monitoring reduces the risk of awareness is unproven, and the cost of using it for this indication is currently unknown.**

THE problem of unexpected awareness has concerned patients and anesthesiologists since the administration of general anesthesia was first described.[1] Indeed, through much of the 19th century, awareness was regarded as an undesirable and unavoidable consequence of the administration of general anesthesia to facilitate surgery. The incidence of awareness was probably low for much of the 19th century, as inhaled agents (ether, chloroform, nitrous oxide) were the sole agents used to administer general anesthesia and were titrated until adequate surgical conditions were obtained. Of note, hypoxia, profound circulatory depression, fire, explosions, and death were all also well accepted and relatively frequent complications of general anesthesia in this era.[2–4] Against this backdrop, the occasional patient who had recall of intraoperative events had a relatively minor problem and a great deal to be thankful for. The incorporation of paralytic agents into the administration of general anesthetics was associated with an epidemic of cases of awareness, as anesthesiologists discovered that these agents did not diminish consciousness in any way.[5–8] The practice of anesthesia has evolved during the past 50 yr, with increasingly safer agents, increasingly reliable monitoring, and increasing scientific understanding of general anesthesia. Death, hypoxia, and shock are now rare events in the operating room compared with the turn of the century.[2,4] However, in recent years, there has been increased attention in the press to the problem of unexpected recall during general anesthetics.

The Bispectral Index (BIS) monitor (Aspect Medical Systems, Natick, MA) has been advocated as a tool that may reduce the incidence of unexpected recall.[10–13] We performed the following power and cost analyses to assess whether this contention could be supported with data currently available and, if so, what the cost of using the monitor solely to prevent awareness would be.

Materials and Methods

Because there is no consensus as to the risk of unexpected awareness in the population of patients undergoing general anesthesia, and because the risk of awareness may vary over a wide range (dependent on the patient population and procedure), we performed all analyses over a wide range of possible rates of awareness.[14,15]

A standard statistical power analysis was performed to determine the size of the randomized, prospective study that would be necessary to demonstrate that the BIS monitor decreases the risk of intraoperative recall. We generated all sample sizes using an 80% power.

A variant of a standard model[16] was created to evaluate the cost of using the BIS monitor. The model, shown in equation 1, can be used to assess the cost of any proposed change in practice intended to reduce the incidence of any phenomenon.

$$\text{Cost} = \text{Price}/(\text{efficiency} \times \text{incidence}) \qquad (1)$$

where price is the marginal cost per use of the monitor, and efficiency is the percentage reduction in the inci-

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Table 1. Sample Size Needed in Both Intervention and Control Groups to Show that the BIS Monitor Reduces the Incidence of Awareness[18]

Postulated Incidence	50% Reduction	90% Reduction
1/100	4,071	1,045
1/500	20,470	5,245
1/1,000	40,969	10,495
1/5,000	204,960	52,498
1/10,000	409,949	105,002
1/20,000	819,927	210,009
1/50,000	2,049,860	525,031

BIS = Bispectral Index.

dence of awareness. In essence, we divided the cost of electrodes by the number of cases of unexpected recall potentially prevented to determine the cost of preventing a single case of this complication. To favor the use of the monitor, we assumed that the cost of the monitor was zero and that there were no other direct or indirect costs associated with its use to prevent awareness (such as purchase cost of monitors, maintenance cost of monitors, costs associated with software upgrades, costs in time to learn how to use monitors, costs in time to interpret and act on results from the monitor). The marginal cost of use is only that of the disposable electrodes, which cost on the order of $10–20 per set (one set per patient is required).

Results

The results of the power analysis are shown in table 1. The results of the cost analysis are shown in table 2.

Discussion

The indiscriminate use of screening tests for low probability events is an extraordinarily expensive proposition.[17] Proving that such screening or testing is effective is a challenging task. It is expensive and must be conducted in an extremely carefully controlled manner to obtain statistically reliable and meaningful results.

The power analysis results presented in table 1 demonstrate that very large sample sizes are required to determine a decrease in the incidence of a rare event such as unexpected recall during general anesthesia.[18] As a consequence of this, it is difficult to assert that any strategy, technique, or monitor reduces the risk of awareness, because proving the assertion is logistically daunting. For example, if the incidence of awareness is as high as 1 in 1,000 and the monitor is 90% effective at preventing awareness, then the trial to demonstrate this would require approximately 21,000 patients. Even if the BIS monitor were extraordinarily effective at reducing the risk of awareness, the number of patients that would need to be studied would be enormous.

Table 2. Cost of Preventing a Single Case of Awareness[25]

	Efficiency	
Postulated Incidence	50% Reduction (US $)	90% Reduction (US $)
1/100	2,000	1,111
1/500	10,000	5,556
1/1,000	20,000	11,111
1/5,000	100,000	55,556
1/10,000	200,000	111,111
1/20,000	400,000	222,222

Because there are cases of awareness in the Aspect database, it is certain that the efficiency of the monitor is less than 100%.[19] As the performance of the monitor decreases (*e.g.*, 50% reduction in awareness as opposed to 90% reduction), the number of patients required in each arm of a study to detect this increases. If the monitor were only 50% effective at preventing awareness instead of 90% effective, the number of patients that would need to be studied increases in the previous example to approximately 82,000.

Demonstrating that the monitor decreases the risk of awareness does become tractable in patient populations at high risk for explicit recall. If the incidence of recall is sufficiently high, and the monitor can truly reduce the incidence of unexpected recall dramatically, then proving that it does should be feasible. For example, if the incidence of recall is 1% in a high-risk patient population such as cardiac, trauma, or obstetrics, and the monitor can be used to reduce the risk of recall by 90%, then a study with slightly more than 2,000 patients would demonstrate this conclusively. Such a study has not yet been reported in the literature.

What will be the effect of monitoring the depth of anesthesia with the BIS on the incidence of awareness? One answer is that it may reduce the risk of awareness.[10–12,20,21] This is more likely to be the case if practitioners use it to assure that patients are experiencing sufficiently deep anesthesia. If practitioners use this monitor to keep patients "just barely" asleep, it may not have as dramatic an impact in reducing awareness and might even increase the risk of awareness. Ironically, the literature that documents reduced drug doses and the associated faster recovery advocates using lighter planes of anesthesia for patients.[20–24] The effect of BIS monitoring on the risk of awareness does require careful consideration of how the presence of the monitor may change the behavior of the practitioners who use it.

Although modestly priced, monitoring techniques used to avert low-incidence complications may have poor cost–benefit characteristics. In the domain of medicine, the indiscriminate use of preoperative tests has been demonstrated to increase costs and, in some cases, worsen outcome. The indiscriminate use of the BIS monitor may demonstrate cost profiles similar to the indiscriminate use of preoperative chest radiographs. Cost

analysis demonstrated that the cost of preoperative chest radiographs in young, healthy patients was likely to be at least $32,500,000 per year of life saved.[17] Monitoring low-risk patients with the BIS monitor may have a similar economic profile (table 2).[25] If the risk of awareness is 1 in 5,000 and monitoring with the BIS reduces the incidence of awareness 90%, then it costs $55,556 to prevent a single case of awareness. If the monitor is only 50% effective at reducing the risk, then the cost to prevent a single case of awareness increases to $100,000. In contrast, the economic profile of using the monitor to prevent awareness in high-risk populations might be favorable. If the risk of awareness is 1% and the monitor is 90% effective, then it costs only $1,111 to prevent a single case of awareness.

Claims for explicit awareness during general anesthesia accounted for only 1.9% of the claims in the closed claims study, with a median payout of $18,000 (range, $1,000–600,000).[26] It is likely that claims and settlements for unexpected recall will increase as a consequence of both inflation and the increased media attention to this problem. Furthermore, because the closed claims data spans a period of decades, during which the payouts for all malpractice claims increased, it is likely that future payouts for awareness suits will be far larger than the average reported in the study. Nevertheless, given the small number of payouts for explicit awareness in the closed claims study and the huge number of anesthetics covered by its insurers, it appears difficult to justify the use of the BIS monitor as a cost-effective way to reduce exposure to malpractice litigation. Indeed, using the data of Domino *et al.*[26] to estimate the frequency of claims (approximately two per year) and the size of payouts for them (highest is $600,000), it is easy to estimate that the cost of the payouts ($1.2 million per year) would be far exceeded by the cost of the electrodes for the groups participating in the Closed Claims Database; $1.2 million would purchase no more than 120,000 electrodes, a small fraction of the cases that would need to be monitored.

There is a substantial literature that suggests that using the BIS monitor to guide the administration of a general anesthetic can reduce expenditure for anesthetic agents, reduce side effects associated with general anesthesia, and reduce the consumption of recovery room resources.[20,22,23,27–30] Most of these studies are not controlled in a manner that allows discrimination as to whether it is the monitor or the anesthetic strategy adopted with its use that is responsible for all of these benefits.

The contention that monitoring the depth of anesthesia with the BIS reduces the risk of awareness remains unproven. Indeed, widespread indiscriminate use of the BIS may actually lead to an increase in intraoperative awareness and increase costs. Until a large study is conducted that proves that the BIS monitor reduces the risk of awareness, statements that this monitor prevents awareness are unproven and, at best, premature. Finally, even if BIS monitoring reduces the risk of unexpected awareness, it may be difficult to justify the expense associated with its use on the basis of this alone.

References

1. Boott F: Surgical operations performed during insensibility (letter). Lancet 1847; 1:5–8
2. Brown DL: Anesthesia risk: A historical perspective, Risk and Outcome in Anesthesia. Edited by Brown DL. Philadelphia, Lippincott, 1988, pp 1–29
3. Keating V: Anaesthetic Accidents: The Complications of General and Regional Anaesthesia, 2nd Edition. Chicago, Year Book Publishers, 1961, pp 270–3
4. Vandam LD: The approach to patient safety in anesthesia: An historical perspective, Patient Safety in Anesthetic Practice. Edited by Morell RC, Eichhorn JH. New York, Churchill Livingstone, 1997, pp 1–21
5. Whitacre RJ, Fisher AJ: Clinical observations on the use of curare in anesthesia. ANESTHESIOLOGY 1945; 6:124–30
6. Prescott F: Tubocurarine chloride as an adjunct to anesthesia. Lancet 1946; 2:80–4
7. Smith SM, Brown HO, Toman JEP, Goodman LS: The lack of cerebral effects of d-tubocurarine. ANESTHESIOLOGY 1947; 8:1–14
8. Smith SM: The use of curare in infants and children. ANESTHESIOLOGY 1947; 8:176–80
9. Winterbottom EH: Insufficient anaesthesia (letter). BMJ 1950; 1:247–8
10. Sebel PS: Central nervous system monitoring during open heart surgery: An update. J Cardiothorac Vasc Anesth 1998; 12:3–8
11. Liu J, Singh H, White PF: Electroencephalographic bispectral index correlates with intraoperative recall and depth of propofol-induced sedation. Anesth Analg 1997; 84:185–9
12. Glass PS, Bloom M, Kearse L, Rosow C, Sebel P, Manberg P: Bispectral analysis measures sedation and memory effects of propofol, midazolam, isoflurane, and alfentanil in healthy volunteers. ANESTHESIOLOGY 1997; 86:836–47
13. Cole P: Doctors waking up to anesthesia's limits: Surgery patients traumatized when drugs fade early, Chicago Tribune. Chicago, 1999, p 4
14. Goldberg M: Awareness during anesthesia, Complications in Anesthesiology, 2nd Edition. Edited by Gravenstein N, Kirby R. Philadelphia, Lippincott-Raven, 1996, pp 425–9
15. Jones JG: Perception and memory during general anaesthesia. Br J Anaesth 1994; 73:31–7
16. Polk S, Roizen M: Cost-benefit analysis in monitoring, Monitoring in Anesthesia and Critical Care, 3rd Edition. Edited by Blitt C, Hines R. New York, Churchill Livingston, 1995, pp 73–94
17. Roizen M: Preoperative evaluation, Anesthesia, 4th Edition. Edited by Miller R. New York, Churchill Livingston, 1994, pp 827–82
18. O'Connor MF, Daves SM, Tung A, Thistead RA, Apfelbaum JL: "Awake during anesthesia": Statistical analysis does not yet support the contention that monitoring depth of anesthesia with the BIS decreases the risk of awareness (abstract). ANESTHESIOLOGY 1999; 91:A1129
19. BIS by Aspect, CD-ROM. Ambler, PA, Aspect Medical Systems, 1999
20. Gan TJ, Glass PS, Windsor A, Payne F, Rosow C, Sebel P, Manberg P: Bispectral index monitoring allows faster emergence and improved recovery from propofol, alfentanil, and nitrous oxide anesthesia. ANESTHESIOLOGY 1997; 87:808–15
21. Song D, Vlymen J, White P: The bispectral (BIS) index predicts fast-track eligibility after ambulatory anesthesia (abstract). ANESTHESIOLOGY 1998; 89:A16
22. Friedberg BL, Sigl JC: Bispectral index (BIS) monitoring decreases propofol usage in propofol-ketamine office-based anesthesia (abstract). Anesth Analg 1999; 88:S54
23. Badrinath S, Avramov MN, Papaioannou ME, Ivankovich AD: The impact of EEG-bispectral index monitoring on drug usage and recovery during ambulatory anesthesia (abstract). Anesth Analg 1999; 88:S51
24. Yli-Hankala A, Vakkuri A, Annila P, Korttila K: EEG bispectral index monitoring in sevoflurane or propofol anaesthesia: Analysis of direct costs and immediate recovery. Acta Anaesthesiol Scand 1999; 43:545–9
25. Daves SM, O'Connor MF, Cook RI, Apfelbaum JL: What is the cost of preventing awareness using BIS monitoring? (abstract). ANESTHESIOLOGY 1999; 91:A489
26. Domino KB, Posner KL, Caplan RA, Cheney FW: Awareness during anesthesia: A closed claims analysis. ANESTHESIOLOGY 1999; 90:1053–61
27. Johansen JW: Learning transference and bispectral index (abstract). ANESTHESIOLOGY 1998; 89:A922
28. Nakatsuka M, Tyler B: Bispectral index monitoring (BIS) to facilitate faster emergence and shorter turnover time for carotid endarterectomy (abstract). Anesth Analg 1998; 86:S221
29. Mayfield JB, Quigley JD: BIS monitoring reduces phase I PACU admissions in an ambulatory surgical unit (ASU) (abstract). ANESTHESIOLOGY 1999; 91:A28
30. Vakkuri A, Kortilla K, Yli-Hankala A: Cost and recovery analysis of outpatient anaesthesia using EEG BIS monitoring (abstract). Br J Anaesth 1999; 82:A.43