

Letters

The Moment of Death



To the Editor:

Most palliative care patients enter a phase of unconsciousness before death. The time from unresponsiveness until death varies, and the decline is occasionally interrupted by episodes of unexpected lucidity even in the final moments of life.¹ Visible evidence includes a fleeting smile, eye opening, gestures, shedding of tears (lacrima mortis), and deathbed visions. These occurrences are sometimes viewed by grieving families with disbelief and a concern their loved one may be distressed. This prospective study used the Bispectral Index monitor (Covidien Pty. Ltd., Lane Cove, New South Wales, Australia) to investigate changes in the Bispectral Index score (BIS) at the moment of death and possible links between this and phenomena observed at the end of life.

The monitor analyzes electroencephalographic (EEG) input from the frontal cortices and converts this by means of an algorithm to a dimensionless BIS that ranges from 100 to 0, where 100 represents full awareness, 50 deep sedation, and 0 brain death.² The technology is a validated means of measuring the level of sedation in anesthetized patients but has not yet been validated outside that setting.

Following ethics approval from the University of Wollongong Human Research Ethics Committee, 30 consenting, eligible, and neurologically intact patients were connected to the monitor from the time they became unresponsive until death. The final 30 minutes of each patient's recording was analyzed for changes in the BIS, electromyographic (EMG) activity, and signal quality (SQ). Our objectives were to ascertain whether there is a significant change in the BIS at the moment of death, the frequency and degree of the change, the influence of EMG activity, depth of sedation, and duration of unconsciousness on the BIS. The study took place in a 15-bed palliative care unit at Port Kembla Hospital, New South Wales, Australia.

Twenty-two (73%) of the 30 patients had a spike in the BIS at the moment of death that exceeded baseline scores by an average of 31 (range 10–65). A

spike of 20 or more (mean 38; range 20–65) was present in 14 patients (46%) of the cohort. The peak BIS was ≥ 90 in four of these patients and ≥ 80 in another six patients. A further eight subjects (27%) had a spike between 10 and 19 (mean 15; range 11–18). A spike was absent or < 10 in the remaining eight subjects. Representative tracings are shown in Figure 1.

The Wilcoxon signed rank test showed a highly significant rise in the BIS at the moment of death ($P < 0.006$) and no change in EMG for the same period ($P = 0.86$). The mean duration of unconsciousness for the 30 patients was 1650 minutes (SD, 1031; range 202–4320 minutes). There was no correlation between the duration of unconsciousness (correlation coefficient 0.18; $P = 0.35$) or depth of sedation as represented by baseline BIS (correlation coefficient 0.132; $P = 0.48$) and the presence of a spike.

All patients received a subcutaneous infusion of an opioid and midazolam throughout the monitoring period. There was no significant correlation between the change in peak BIS at the moment of death and the dose of opioids or midazolam (opioids: correlation coefficient 0.23, $P = 0.23$; midazolam: correlation coefficient -0.03 , $P = 0.89$). A small number of patients received additional subcutaneous phenobarbitone and/or clonazepam and/or hyoscine hydrobromide by infusion or regular injection. A BIS spike was present in all but one of the nine patients receiving hyoscine hydrobromide (mean 31; range 10–51), 60% of those receiving clonazepam (mean 46; range 27–65), and 75% who received phenobarbitone (mean 31; range 16–47).

The finding of an increase in the BIS equal to or greater than 20 at the moment of death in 46% of subjects is striking. This figure is similar to that of the only other comparable palliative care study, which noted a spike in more than half of the 58 subjects studied.³ Why the spike occurs in some but not all patients is unclear, but opioids, midazolam and hyoscine hydrobromide, appear to not play a part. The same may be true for phenobarbitone and clonazepam, but circumstantial evidence suggests the effect of both drugs may be related to their dose and duration of use.

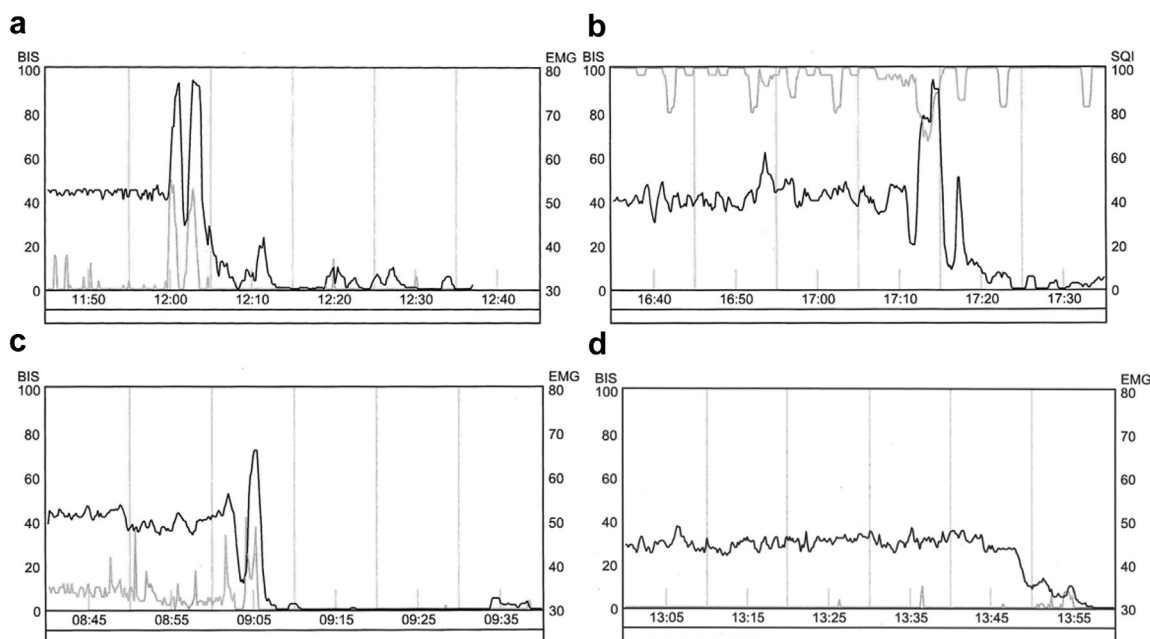


Fig. 1. Representative tracings of BIS plus EMG (a, c and d) and BIS plus SQI (b) around the time of death. Each tracing is 60 minutes in duration. This research focused on the 30 minutes before and including the spike or fall in BIS (moment of death). BIS = Bispectral Index score; EMG = electromyographic activity; SQI = signal quality index.

Signal pollution from excessive EMG activity as a consequence of undersedation and opioid-induced muscular rigidity remains the most common source of falsely elevated BIS outside the anesthetic setting.⁴ Although there is no consensus concerning the maximum EMG that can be tolerated, we adopted the custom of excluding BIS when EMG >50 Hz. This precautionary measure, the absence of a significant EMG change at the time of death, and an equivalent level of sedation in all patients make EMG interference an unlikely cause of the spike within our cohort.

Despite some scores reaching levels usually associated with almost full arousal, none of our subjects showed signs of being awake or aware. There was, however, one patient who, after many hours of unresponsiveness, suddenly opened his eyes and made several gesturing movements immediately before death. His data were excluded from the study because of poor SQ and raised EMG related to the movement.

The finding of a BIS spike at the moment of death is not new. To the best of our knowledge, this phenomenon was first reported in 2001,⁵ and although there is considerable speculation about its significance, the reason for its appearance has not been established. The frequent and consistent appearance of the spike, however, has led to the view that it is not an artifact or easily explained by a change in the EMG.^{6,7}

Anecdotal reports of patients dying in intensive care or during the procedure of donation after cardiac death have shown a transient surge of

neurophysiological activity usually indicative of cerebral arousal. This was noted at the exact time of the BIS spike and dissipated as the spike waned.^{7,8} In most, but not all instances, this neurophysiological change occurred when the patients were asystolic. Uncertainty exists as to the cause and significance of this finding, but one author has suggested that it may be responsible for the near-death experience described by some patients who are successfully resuscitated after a cardiac arrest.⁶

Given this, it is tempting to suggest that the BIS spike and neurophysiological changes responsible for it may represent a qualitative change in consciousness at the moment of death rather than the agonal throes of a dying brain. This same neurophysiological change may account for some of the end-of-life experiences including deathbed visions. This hypothesis is supported by animal studies that show that neural correlates of heightened conscious processing are generated at near death.⁸

The major limitation of this study arose from our desire to respect the privacy of the patient and his and/or her family and to honor the significance of the dying experience by limiting the degree of intrusion. Having said that, none of the subjects' relatives asked for the monitoring to cease, and all expressed an interest in the study and its outcomes. The other significant limitation is the unproven reliability and validity of the Bispectral Index monitor outside the anesthetic situation and the absence of raw EEG data to substantiate our findings.

Although this study confirms the frequent occurrence of a spike in the BIS at the moment of death, the absence of raw EEG data prevents us from adding to the discourse about its genesis. It does, however, present evidence against the spike being an artifact and shows that appropriate doses of most commonly prescribed end-of-life medications do not prevent its appearance. Although ethically challenging, further studies may help to unravel the mystery that surrounds the moment of death and remove the heavy silence that has fallen over the subject of death.⁹

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Inferring Palliative Intent From Administrative Data: Validation of a Claims-Based Case Definition for Venting Gastrostomy Tube



To the Editor:

Malignant bowel obstruction (MBO) is associated with limited survival and a high burden of suffering in patients with incurable intra-abdominal malignancies.¹ The prevalence of MBO is estimated to be 3% to 15% in patients with cancer.² Early evidence suggests that palliative treatment with venting gastrostomy tube (VGT) alleviates symptoms and facilitates hospital discharge.³ However, the literature predominantly consists of small single-institution observational studies. Outcomes data from large population-based studies are needed to inform management decisions for MBO. At present, procedure and diagnosis codes from *The International Classification of Diseases, Ninth Revision* (ICD-9) and Current Procedural Terminology neither identify intestinal obstruction caused by malignancy, nor do they distinguish VGT from those indicated for feeding. This poses a major barrier to using medical claims data to conduct such studies.

We hypothesized that because the presence of a bowel obstruction is a contraindication to feeding gastrostomy tube placement, gastrostomy tubes placed during hospitalization for bowel obstruction in patients with cancer are indicated for venting. The present study examined the validity of this case definition through medical record review with the goal of defining procedure and diagnosis codes that could be used to identify VGT placement for MBO in administrative data.

Methods

Data Source and Study Cohort

Administrative patient data were obtained from the Research Patient Data Registry, a centralized repository of patient encounters at two large academic medical centers.⁴ This was used to identify the cohort and obtain medical record numbers, demographic data, and diagnosis and procedure codes associated with the hospital stay. Medical record numbers were used to review procedure notes (operative, endoscopy, or interventional radiology reports) and progress notes. The cohort consisted of patients 18 years and older who underwent gastrostomy placement (ICD-9-CM 43.11, 43.19, and 44.32; Current Procedural Terminology 49440) as an inpatient procedure from January 2012 to March 2016 and had one or more malignancy diagnosis codes (ICD-9-CM 140-209) during admission or in the prior 180 days.