

## Extended glasgow outcome scale and correlation with bispectral index



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### ABSTRACT

Traumatic brain injury (TBI) is a major public health issue, which results in significant mortality and long-term disability. The profound impact of TBI is not only felt by the individuals who suffer the injury but also their caregivers and society as a whole. Clinicians and researchers require reliable and valid measures of long-term outcome not only to truly quantify the burden of TBI and the scale of functional impairment in survivors but also to allow early appropriate allocation of

rehabilitation supports. In addition, clinical trials which aim to improve outcomes in this devastating condition require high-quality measures to accurately assess the impact of the interventions being studied. In this article, we review the properties of an ideal measure of outcome in the TBI population. Then, we will describe the measurement tools include: the Glasgow Outcome Scale (GOS) and extended Glasgow Outcome Scale (GOSe) in correlation with bispectral index (BIS).

### Keywords:

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### INTRODUCTION

Traumatic brain injury is a frequently recorded case in the Emergency Department. Traumatic brain injury is one of the main causes of death in the range of productive age. Globally traumatic brain injury incidents are increasing sharply due to increased use of motor vehicles. According to World Health Organization (WHO) estimates, by 2020 traffic accidents will be the third most prevalent cause of illness and trauma in the world. Every year about 5.3 million Americans suffer brain injuries. While in Europe in 2010 the incidence of traumatic brain injury reached 500 per 100,000 population. Traumatic brain injury is a mechanical trauma that directly or indirectly affects the head which can lead to impaired neurological function, even death. In general, traumatic brain injury results from motor vehicle accidents, attacks or crimes, violent blows, gunfire, or improper movement during exercise. An awareness level assessment is important in patients with traumatic brain injury because the level of consciousness is one of the parameters important for clinicians in making decisions when determining therapy or intervention. Accuracy in the assessment of the degree of awareness is very important because if there is a mistake in determining the degree of awareness it will be able to influence the management of therapy and also outcome from the patient.<sup>1</sup>

The BIS Monitor, a tool that used to objectively assess the level of awareness, was introduced in 1994 by Aspect Medical Systems (USA) as a

modality to measure the level of patient awareness during general anesthesia based on the bispectral analysis of electroencephalogram (EEG). BIS values range from 0 (isoelectric signals) to 100 (conscious patients). The depth of anesthesia that is considered sufficient for surgery ranges from 40-60. The use of current BIS monitors has also been widespread in the Intensive Care Unit (ICU) to monitor the effects of sedation. Patients with Traumatic brain injuries lead to disability and even death, so it is deemed necessary to assess outcomes in brain-injured patients treated in hospital. The final outcome assessment of patients with head injuries is using Glasgow Outcome Scale (GOS) and extended Glasgow outcome scale (GOSe). Assessment using GOS and GOSe is gaining popularity and is often used in developed and developing countries to assess the outcomes of patients with brain injury who are treated in hospital.<sup>2</sup>

### Functional measurement scales commonly used in TBI patients

There are a wide number of scales that have been developed to assess function, handicap, and disability following TBI. These 'functional' scales aim to assess objectively the burden that TBI may impose on a patient's life. We conducted a MEDLINE search of studies involving assessment of functional and quality of life outcomes in patients with TBI to identify the most commonly used assessment scale. Glasgow Outcome Scale (GOS) and extended Glasgow Outcome Scale (GOSe) originally

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described in 1975, the Glasgow Outcome Scale (GOS) has become the most widely used method for classifying outcome in TBI survivors.<sup>3</sup> It is used by both acute care and rehabilitation specialists to assess recovery.<sup>4</sup> The GOS is a multi-dimensional scale which assesses various aspects of outcome (i.e., consciousness; independence; work status; return of lifestyle). The five categories of the original GOS scale are: (i) dead; (ii) vegetative (cannot interact, unresponsive) and (iii) severely disabled (can follow commands, cannot live independently); moderately disabled (can live independently, reduced work capacity) and good recovery (can work).<sup>5</sup> The output from the scale is frequently dichotomised into unfavorable (dead, vegetative and severely disabled) versus favorable (moderately disabled and good recovery) outcomes. The scale reflects the impact of the TBI on the patient's level of functioning. The GOS has proven as a useful and simple measure and has been used in many clinical trials to assess outcomes in patients with moderate and severe TBI.<sup>6</sup>

Despite its widespread use, the GOS is increasingly recognized to have a number of important inadequacies, some of which relate to the simplicity of the scale.<sup>7</sup> These limitations include a perceived allocation bias in the higher functional end of the scale, evidence of systematic bias between different professional groups administering the scale, and the 'open ended' and unstructured format of the interview used by some. These shortcomings have led to speculation that the GOS is insensitive to small (but clinically relevant) changes in functional status.<sup>8</sup> These concerns about loss of sensitivity in part lead to the development of an extended version of the scale (GOSe) which separates each of the three higher function categories into two, making eight categories in total. It has been prospectively demonstrated that the validity (criterion) of the GOSe generally exceeds the GOS and it is more sensitive to change than the GOS.<sup>7</sup> Outcomes as determined by the GOSe are strongly associated with outcome category on numerous alternative functional scales. These findings lend further support for utilization of the GOSe over the original GOS in clinical trials. Many of the other previous criticisms of both the GOS and GOSe have been addressed by the development of a structured interview process; under these conditions the GOS and GOSe have good reliability<sup>7</sup> in patients with TBI. The reliability of this scale when administered by phone call (as opposed to face-to-face interview) is an additional feature which increases the practical usefulness of this measure. A recent expert workshop sponsored by the National Institute of Neurological Disorders

and Stroke recommended the use of the GOSe as the gold standard outcome measure in future TBI trials. However, the optimal method of analysis of the GOS/GOSe has been more controversial. While it is widely acknowledged that the dichotomization of any scale reduces its sensitivity, the majority of studies continue to use the dichotomized version of the GOS/GOSe as their primary outcome measure. Many feel that it is better to exploit the ordinal nature of the GOS/GOSe scales and relate the outcome to the risk for individual patients. Two different approaches for this are the proportional odds analysis model (estimate of the shift in outcome across the GOS/GOSe scale) and the sliding dichotomy (the point of the dichotomy of the GOS/GOSe is differentiated according to the baseline risk estimated in each individual patient). Initial reports of the use of these methods have been encouraging, and have led to recommendations for future clinical trials to switch from the conventional dichotomized GOS/GOSe analysis to these newer models.<sup>9</sup>

It is clear that the earlier an outcome tool can be reliably and validly used to assess a cohort of patients the more useful it will be, not only to give early information to caregivers but also to prevent drop-out and loss to follow-up in clinical trials. However, the use of any tool in patients with TBI needs not only to balance these logistic demands but also to recognize that a reasonable period of time is needed for improvement and stabilization of recovery before assessment. Most studies have used the GOS/GOSe at 6–12 months post injury. While there may be a small change in the proportion of patients with good recovery at 6–12 months, the dichotomised 'favorable' versus 'unfavorable' outcome has generally stabilized at this stage.<sup>32</sup> While it is recognized that this 6–12 months assessment may not be the 'final' outcome state it is used by many studies which assume that any disability persisting at this stage is permanent or life-long. This point is important when one is tracking recovery. It is also important to note that changes in outcome in an individual patient between 6 months and 1–2 years post injury may reflect the level and quality of rehabilitation support rather than the deficit from the initial injury. This is a finding which is important to document especially in the context of multi-national clinical trials where the quality of rehabilitation could differ significantly. Conversely, it is also vital to recognize the potential bias introduced when very early assessments (i.e., GCS) are made to predict long-term outcomes after TBI, given the potential confounding effects of inadequate volume resuscitation and alcohol intoxication.<sup>3</sup>

### Bispectral Index (BIS)

During the evolution of modern anesthesia practice, the assessment of anesthetic depth in patients has undergone gradual changes and improvement. Observation of previous anesthesia depth from clinical signs such as pupil response, respiratory pattern, pulse quality plus direct measurement of physiological endpoints including blood pressure, heart rate and respiratory rate and respiratory volume. With the development of pulse oximetry and capnography, proper assessment of ventilation management is enforceable. The use of end-tidal and peripheral nerve stimulation give the anesthesiologist the ability to measure the concentration of pharmacological agents and the effects of each drug. Currently, heart function can be evaluated using advanced technology of pulmonary artery catheters and transesophageal echocardiography (TEE) for new methods of continuous blood pressure and cardiac monitoring.<sup>10</sup>

Despite the remarkable developments in the assessment of cardiovascular systems during anesthesia, the direct determination of the effects of anesthesia and sedative on the central nervous system remains a challenge. Careful clinical investigation shows that the hemodynamic response does not always provide an accurate representation of the central nervous system response to anesthetic agents and therefore unreliability of brain status indicators. In contrast, a technology that will allow independent neurophysiological monitoring of the central nervous system will provide a direct measure of brain status during anesthesia and sedation, allowing physicians to perfect perioperative management and achieve the best outcomes for each patient. Accurate monitoring and targeting effects on the brain, in combination with traditional clinical assessment and monitoring assessments, will enable a more complete approach to adjusting doses and mixtures of anesthesia, sedatives and analgesic agents.<sup>11</sup>

The Bispectral Index Monitor (BIS) initially appears to assist professional anesthesiologists as a direct and accurate method of continuously monitoring brain activity throughout the course of anesthesia and surgery. BIS monitors are considered capable of providing measurements on the hypnotic effects of anesthetic drugs. BIS is the first tool capable of quantitatively providing an EEG picture. BIS tools consist of sensors, digital signal modifiers, and monitors. The sensor is placed on the patient's forehead to pick up electrical signals from the cerebral cortex and transfer them to the digital signal changes. This BIS

monitor is able to integrate various mark of EEG into single variable. Artifacts on BIS may occur when there is electrical activity arising from sources other than the brain, such as other body parts (eg eye movements and jaw movements), environment, or equipment.<sup>10,11</sup>

It has been known for decades that EEG changes in response to the effects of anesthesia. Although each drug can induce some unique effects on the EEG, the overall pattern of EEG wave changes is very similar to each other. One of the primary goals in developing brain-status monitoring technology is to identify EEG features that are strongly associated with sedation or hypnosis caused by commonly used anesthetic agents. In its development, this BIS can then also be used to monitor brain electrical activity in patients treated in ICU, predicting neurological outcomes of patients, giving Picture the level of awareness in patients with traumatic brain injury, and estimate prognosis in coma patients, BIS scores are considered capable of reflecting the functional status of the cerebral cortex.<sup>11</sup>

The numbers appearing on the BIS monitor are obtained by utilizing a mixture of various EEG signal processing techniques including bispectral analysis, spectral power analysis, and time domain analysis. These steps are combined through an algorithm to optimize the correlation between EEG and clinical effects of anesthesia. Due to the sophisticated and intricate process of this analysis, the score that appears on the BIS monitor does not reflect the condition of brain activity in real time. There is a delay time of approximately 15-30 seconds of signal acquisition until the BIS score of the data appears on the BIS monitor.<sup>12</sup>

The BIS index is the result of processing of BIS algorithms. The bispectral analysis is part of the cortical EEG picture that describes the changes that occur in the relationship between the neural generators in cortical and subcortical. If the cortical-sub-cortical relationship is altered, then there will be a change of pattern on the EEG. The bispectral analysis has a complex method of signal processing that assesses the relationships between the components that change due to the change in received signal and then synchronizes the changes in the signal. By quantifying the relationship between all frequencies generated by the signal, the bispectral analysis is capable of generating additional descriptors of EEGs that describe brain activity during the hypnotic phase. BIS algorithm obtained from the observation of more than 5000 subjects who get a particular hypnotic agent. Various modalities are used to assess the sedation effects of the drug simultaneously. One

of the key modalities in the assessment is the EEG picture. From these observations, it is hoped that the discovery of one or more key features (also called 'predictors') is strongly correlated with sedation or hypnosis. Data of observation result are then analyzed with multivariate test to assess correlation among variables.<sup>12</sup>

Research by Paul and Rao in 2006, found that BIS has a significant correlation to GCS in cases of traumatic brain injury ( $r = 0.67$ ,  $p < 0.001$ ). The average BIS score is reported to increase as the GCS score increases. The mean value of BIS in CKR patients was  $65.7 \pm 16.1$  and in CKS was  $86.7 \pm 6.1$ . While Jung (2013) found that the mean values of BIS in comatose, semi-coma, stupor, and drowsiness were seen respectively  $0.14 \pm 0.23$ ,  $38.9 \pm 18.0$ ,  $60.3 \pm 14.5$ , and  $73.6 \pm 16.5$ . This suggests that the use of BIS is not only limited to anesthesia but may also be used to assess the extent of brain electrical activity in traumatic brain injury patients. If the correlation between BIS and GCS is strong, then the reporting and communication process between future medical personnel will be universal and more objective than using GCS scores alone.<sup>13</sup>

### Correlation Glasgow outcome scale and bispectral index

Many studies say there is a significant relationship between the value of BIS and GOS / GOSE. Hana et al, have studied 25 patients ages 18-75 (av. 36) y. Head injury was severe (initial GCS  $< \text{or} = 8$  in 18 patients, and moderate (initial GCS 9-12) in 7 patients. Daily assessment included GCS and BIS evaluation during the first-week post-injury. Glasgow outcome scale (GOS) was used to assess outcome at discharge. GOS scores were compared to average BIS (obtained from the area under the curve for BIS x time/total time) for 7 days post injury and av. GCS for 7 days post injury. Daily BIS values were also compared to simultaneously recorded GCS. Data were analyzed by Spearman rank correlation analysis; GOS was ranked as 1 to 5 for good recovery (GR), moderate disability (MD), severe disability (SD), persistent vegetative state (PVS), and death, respectively. There were strong correlations between GOS and BIS. BIS  $> \text{or} = 60$  was associated with good outcome, whereas, an av. BIS  $< \text{or} = 40$  was associated with poor outcome.<sup>14</sup>

### Conclusion

It is clear that many patients suffer significant disability following TBI. There are a number of scales which are commonly used to assess disability,

impairment, and function as well as the quality of life measures. The GOSe at 6 months is the most reliable, validated and commonly used functional outcome measurement scale in randomized controlled trials of patients following TBI. In addition, the conventional straight dichotomy analytic technique, whilst more commonly utilized, is less sensitive than either the proportional odds or sliding dichotomy techniques, which are likely to become the standard in the future. A valid measuring instrument and can objectively measure the level of consciousness before assessed the outcome after getting therapy is bispectral index. Many studies have suggested a positive correlation between BIS and GCS in measuring awareness of patients with traumatic brain injury, and a strong correlation between BIS score and GOS score so that BIS can predict the outcome of patients with traumatic brain injury.

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