Turk J Intensive Care 2023;21:1-7
DOI: 10.4274/tybd.galenos.2022.08379

ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

Kutlay Aydın,
Yasin Levent Uğur,
Taner Çalışkan,
Begüm Ergan,
Tuğçe Mengi,
Yusuf Savran,
Erdem Yaka,
Bilgin Cömert,
Uğur Koca,
Pembe Keskinoğlu,
Ali Necati Gökmen

Usefulness of Bispectral Index Monitoring for the Detection and Diagnosis of the Brain Death

Beyin Ölümü Tespiti ve Tanısında Bispektral İndeks Monitorizasyonunun Yararlılığı

Received/Geliş Tarihi : 08.07.2021
Accepted/Kabul Tarihi : 01.04.2022

Kutlay Aydın, Yasin Levent Uğur, Taner Çalışkan, Begüm Ergan, Tuğçe Mengi, Yusuf Savran, Bilgin Cömert, Uğur Koca, Ali Necati Gökmen
Dokuz Eylül University Faculty of Medicine, Intensive Care Unit, İzmir, Turkey

Erdem Yaka
Dokuz Eylül University Faculty of Medicine, Department of Neurology, İzmir, Turkey

Pembe Keskinoğlu
Dokuz Eylül University Faculty of Medicine, Department of Biostatistics and Medical Informatics, İzmir, Turkey

Kutlay Aydın MD, (✉),
Dokuz Eylül University Faculty of Medicine, Intensive Care Unit, İzmir, Turkey

E-mail : kutlayaydin@hotmail.com
Phone : +90 532 264 92 94
ORCID ID : orcid.org/0000-0003-2469-2833

Presented in: This study was presented at the 22nd International Congress of Intensive Care in 2019, in İstanbul.

ABSTRACT *Objective:* Bispectral index (BIS) is a parameter generated from a mathematical analysis of frontal cortex activity. BIS monitoring has been widely used in cerebral pathologies such as traumatic brain injury, brain death, metabolic coma and barbiturate coma and some studies have reported a good correlation between neurological status and BIS values. We evaluated the validity of BIS monitoring for the detection and diagnosis of brain death in our study.
Materials and Methods: Our study was a methodological prospective study. Twenty-eight patients with severe coma [Glasgow coma scale score (GCS)<8] at intensive care unit (ICU) admission are monitored by BIS. Eight patients were excluded from the study due to varies reasons. Data of twenty patients with brain death were evaluated.
Results: The most common diagnoses were intracranial hemorrhage (8 patients-40%) and subarachnoid hemorrhage (8 patients-40%). The most common used ancillary method was computed tomography angiography. BIS and suppression ratio (SR) were determined as 0 and 100 respectively at the moment of brain death diagnosis in 12 of 20 patients, whereas BIS was determined >0 in the remainders. When the receiver operating characteristic curve analysis was performed for the 34041 BIS values of 20 patients, the area under curve was found as 0.582 (0.576-0.588), which was statistically significant (p<0.05). There was a strong negative correlation between BIS and SR and it was statistically significant (R:-0.959, p<0.05).
Conclusion: BIS is a non-invasive method and it may be used in the ICU. BIS monitoring may be useful, especially in patients with head trauma and GCS =3. BIS monitoring provides information about the neurological prognosis. We consider that BIS monitoring can prevent the loss of time by providing to detect the moment of the brain death and thus facilitating the organ transplantation process and however it can not take the place of the other ancillary methods.
Keywords: Bispectral index monitoring, brain death, ancillary method

ÖZ *Amaç:* Bispektral indeks (BİS) frontal korteks aktivitesinin matematiksel analizi ile elde edilen bir parametredir. BİS monitorizasyonu travmatik beyin hasarı, beyin ölümü, metabolik koma ve barbitürat koması gibi serebral patalojilerde yaygın olarak kullanılmaktadır ve bazı çalışmalar nörolojik durum ve BİS değerleri arasında iyi bir korelasyon olduğunu bildirmektedir. Çalışmamızda BİS monitorizasyonunun beyin ölümü tespiti ve tanısındaki geçerliliğini incelemeyi amaçladık.
Gereç ve Yöntem: Çalışmamız metodolojik prospektif bir çalışmadır. Ağır komalı [Glasgow koma skala skoru (GKS)<8] 28 hastaya yoğun bakım ünitesi (YBÜ) kabulü ile birlikte BİS monitorizasyonu uygulandı. Sekiz hasta farklı sebeplerle çalışmadan çıkartıldı. Beyin ölümü tanısı olan 20 hastanın verileri değerlendirildi.
Bulgular: En sık görülen tanı intrakraniyal kanama (8 hasta-%40) ve subaraknoid kanamaydı (8 hasta-%40). En sık kullanılan yardımcı yöntem bilgisayarlı tomografik anjiyografiydi. Yirmi hastanın 12'sinde beyin ölümü teşhis anında BİS 0 ve supresyon oranı (SR) 100 olarak bulundu. Geri kalan hastalarda BİS >0 olarak tespit edildi. Yirmi hastanın 34041 BİS değeri için alıcı işletim karakteristik eğri analizi yapıldığında eğri altındaki alan değeri 0,582 (0,576-0,588) olarak bulundu ve istatistiksel olarak anlamlıydı (p<0,05). BİS ve SR arasında istatistiksel olarak anlamlı olan güçlü negatif korelasyon vardı (R:-0,959, p<0,05).
Sonuç: BİS non-invaziv bir metottur ve YBÜ'de kullanılabilir. BİS monitorizasyonu özellikle GKS =3 olan kafa travmalı hastalarda yararlı olabilir. BİS monitorizasyonu nörolojik prognoz hakkında da bilgi vermektedir. BİS monitorizasyonunun beyin ölümü anının tespitini sağlayarak zaman kaybını önleyeceğini ve organ transplantasyon sürecini hızlandıracağını ancak diğer yardımcı yöntemlerin yerini alamayacağını düşünüyoruz.
Anahtar Kelimeler: Bispektral indeks monitorizasyonu, beyin ölümü, yardımcı yöntem

Introduction

It is among the duties and responsibilities of intensive care physicians in our country as well as in the world to determine and report brain death which means the end of life medically and legally (1). Brain death is a clinical diagnosis of irreversible loss of cerebral hemisphere and brainstem functions. There are three fundamental findings in brain death. These include the presence of irreversible coma, absence of brainstem reflexes, and positive apnea test characterized by the absence of respiratory response to severe hypercapnia (2,3).

Ancillary tests are essential legally to confirm the brain death in some countries when brain death is suspected or prediagnosed clinically (4). Electrophysiological studies [electroencephalography (EEG), somatosensory evoked potentials] and tests measuring cerebral blood flow [cerebral angiography, computed tomography angiography (CTA), transcranial Doppler ultrasonography (TCD), radionuclide cerebral scintigraphy] are used as ancillary tests (3). Cerebral angiography is considered to be the most important test evaluating cerebral circulation (5). In cases where a clinical diagnosis of brain death is made, an ancillary test evaluating the cerebral circulation is performed and if this test is compatible with brain death, there is no need for a second neurological examination (3). Thus, an ancillary test seems to be a more practical way to save time in the diagnosis of brain death. The requirement to transfer the patient out of the intensive care unit (ICU) for these procedures carries a risk for the patients. In addition, the use of contrast media during cerebral angiography may potentially jeopardize the kidney and other organs of the potential donor candidate (4,5).

Bispectral index (BIS) monitoring, approved by the United States Food and Drug Administration for the measurement of hypnotic effects of anesthetics and sedative drugs in 1996, was developed for the measurement of sedation depth and consciousness level during and after general anesthesia. BIS monitoring, which has expanded in use over time, has been widely used in cerebral pathologies such as traumatic brain injury (TBI), brain death, metabolic coma and barbiturate coma (6,7). BIS is a parameter generated from mathematical analysis of frontal cortex activity with 2-channel EEG. BIS values are between 0 and 100, 100 means complete conciousness, 0 means full electrical silence of the brain (8). BIS values between 65-85 means appropriate sedation level (7). It is stated that BIS monitoring is a noninvasive method and can be used in ICU for the measurement of sedation depth (9). Some studies have reported a good correlation between neurological status and BIS values in non-sedated comatose patients (10,11). Dunham et al. (12) reported that BIS monitoring in head trauma patients with a low Glasgow coma scale score (GCS) may be useful to determine the appropriate timing for a comprehensive neurological examination, apnea assessment, or an ancillary test. Vivien et al. (10) suggested that BIS monitoring could be used to ensure proper programming of EEG and cerebral angiography to confirm brain death by determining the onset of brain death in comatose patients. Okuyaz et al. (13), in their study, reported that decreasing BIS to 0 in patients with suspected brain death may support the brain death diagnosis in children and thus that expensive tests such as cerebral angiography can be planned at the appropriate time. We aimed to evaluate the validity of BIS monitoring for detecting and diagnosis of brain death in our study.

Materials and Methods

Study Groups

Our study is a methodological prospective study to determine the validity of BIS application in the clinical course of coma patients and the diagnosis of brain death. Study was performed between 2016-2017 in Dokuz Eylül University (DEU) Faculty of Medicine ICU after DEU Non-Interventional Research Ethics Committee approval (decision no: 2016/19-05, date: 14.07.2016). No additional consent was obtained from the patient relatives for the study.

Twenty-eight patients admitted to our clinic with severe coma (GCS <8) due to TBI, spontaneous intracranial hemorrhage (ICH), subarachnoid hemorrhage, ischemic stroke and hypoxic brain injury were included in the study. Eight patients were excluded from the study, because 3 patients without brain death diagnosis were died, 3 patients were not diagnosed with brain death and BIS records of 2 patients were not appropriate. Data of 20 patients with brain death were evaluated (Figure 1). The cause of the coma in each patient was evaluated and patients with reversible coma reasons (hypothermia, hypovolemic or hypotensive shock, intoxications, barbiturate or other sedative-narcotic drugs, metabolic disorders) or impaired forehead integrity were not included in the study.

All patients included in the study were followed-up for possible brain death. Critical cares of patients with brain trauma in ICU were performed according to the standard

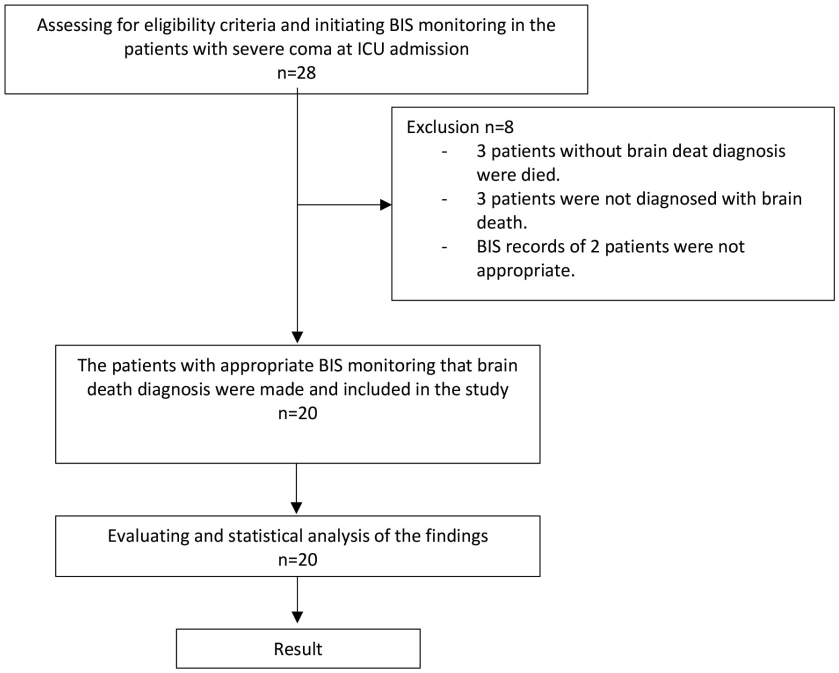

Figure 1. Study flow-chart
BIS: Bispectral index, ICU: intensive care unit

procedures of Brain Trauma Foundation Guidelines (14) and BIS monitoring was performed in all patients included in the study. The skin was cleaned before placing the BIS sensor and BIS sensors were used for a maximum of 72 hours. Sensors were changed if necessary.

Neurological examination was performed at 6 hour intervals each day. If clinical findings were not consistent with brain death, monitoring was continued as afore planned. But if a patient showed GCS regression, the neurological examination was performed hourly. Clinical evaluation of brain death was performed in patients with suspected brain death in the neurological examination. CTA, TCD, and digital subtraction angiography (DSA) were performed as an ancillary test in patients who were both clinically compatible with brain death and in whom apnea test positive. Consistency of BIS values with the brain death diagnosis was evaluated in patients whose brain death diagnosis was confirmed by an ancillary test. A significant change in BIS values accompanying GCS regression and its association with prognosis were also evaluated.

Brain Death Diagnosis

The brain death diagnosis was performed by the absence of brainstem reflexes and apnea test positivity in patients with irreversible coma according to the recommendations of the Ministry of Health Organ and Tissue Transplantation Services Regulation updated in 2014 (01.02.2012-28191) (15).

Data Collection

Demographic data, cause of coma, GCS and neurological examination findings at the admission of 28 patients were recorded. BIS monitorization was started in all patients admitted to ICU and neurological examination was done routinely every six hours, but upon regression of GCS of the patient, neurological examination frequency was increased and performed every hour. Suppression ratio (SR), signal quality index (SQI) and electromyographic activity (EMG) were recorded by BIS monitoring continuously.

BIS Monitoring

BIS and EMG of patients were monitored continuously by VISTA device (Aspect Medical System Inc., MA, USA). Four channel sensor (Quattro, Aspect Medical System Inc., MA, USA) was used in BIS device. Data were transferred to a computer for analysis and artifacts generated by devices such as cardiac pacing and air heating systems that could affect BIS recordings were removed.

Statistical Analysis

In our study, when the power analysis for receiver operating characteristic (ROC) with 80% power, 95% confidence interval and area under curve (AUC) =0.75, the number of samples to be included in the study was calculated as 20. For correlation analysis, 80% power 95% confidence interval and 0.70 correlation between two measurements were found to be 23 samples.

Data obtained from the patients were expressed as mean ± standard deviation if showed normal distribution in continuous characteristics, and median [minimum-maximum (min-max)] if not a normal distribution. The normal distribution of data was evaluated by the Kolmogorov-Smirnov test. Categorical data were defined by frequency and percentages.

In order to determine the validity of BIS, the clinical and ancillary test and brain death decision were accepted as the gold standard reference, the statistical significance of AUC obtained from ROC curve analysis for BIS values of 20 patients at the time of brain death diagnosis was tested. 34041 repeated BIS measurement data of 20 patients were evaluated. The optimal cut-off point was determined from the ROC curve for BIS with the highest sensitivity and specificity, and sensitivity and specificity values were determined according to this point. Spearman correlation analysis was performed between BIS and SQI, SR, EMG values. In the Spearman correlation $p<0.01$ and in the other evaluations $p<0.05$ were considered statistically significant.

Results

Mean age of 20 patients (13 males and 7 females) in the study was 61.9±17.7 years. Mean ICU length of stay was 4.1±5.6 days. The most common diagnosis at ICU admission were ICH (8 patients-40%) and subarachnoid hemorrhage (8 patients-40%). Mean GCS of patients with brain death at ICU admission was 3.3±0.9 (Table 1). The most common used ancillary method for the brain death diagnosis was CTA [75% (n=15)]. TCD was used in 2 patients (10%) and DSA was used in 1 patient (5%). Also two patients (10%) were diagnosed with brain death without ancillary test.

BIS and SR were determined as 0 and 100 respectively at the moment of brain death diagnosis in 12 of 20 patients, whereas BIS was determined >0 in the remainders. BIS median value was identified 0 (min-max 0-69) at the moment of brain death diagnosis. The median (min-max) values of BIS, SQI, EMG and SR data were as follows; 0 (0-97), 100 (0-100), 26 (20-80), 100 (0-100). 34041 repeated BIS measurement data of 20 patients were evaluated. In order to determine the validity of BIS, the clinical and ancillary tests and brain death decision were accepted as gold standard, when the ROC curve analysis was performed for the BIS values of 20 patients at the moment of brain death diagnosis, the AUC was found as 0.582 (0.576-0.588) which was statistically significant ($p<0.05$) (Figure 2). The sensitivity and specificity of ROC curve analysis for BIS were 0.752, 0.384 consecutively and the optimal diagnostic value

Table 1. Demographic and clinical information of patients

Characteristics	**n=20**
Age (years) (mean ± SD)	61.9±17.7
Gender n (%)	
Male	13 (65%)
Female	7 (35%)
GCS (at ICU admission) (mean ± SD)	3.3±0.9
Time from ICU admission to brain death (days) (mean ± SD)	3.4±5.6
Hospital lenght of stay (days) (mean ± SD)	6.4±5.7
ICU length of stay (days) (mean ± SD)	4.1±5.6
Diagnosis n (%)	
ICH	8 (40%)
ICM	1 (5%)
SAH	8 (40%)
Methanol intoxication	2 (10%)
Firearm injury	1 (5%)

GCS: Glasgow coma scale score, SD: standard deviation, ICU: intensive care unit, ICH: intracranial hemorrhage, ICM: intracranial mass, SAH: subarachnoid hemorrhage

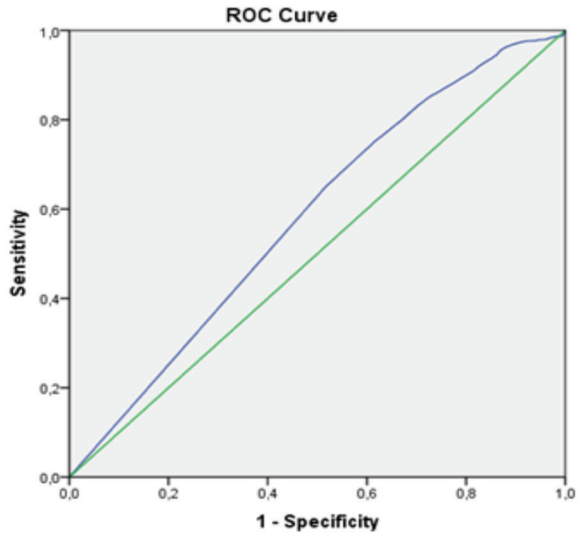

Figure 2. ROC curve of BIS measurements for brain death decision
BIS: Bispectral index, ROC: receiver operating characteristic

was 1.5. There was a negative correlation between BIS and SQI and it was statistically significant (R: -0.118, p<0.05). Although there was a statistically significant correlation, since R<0.20, there was no mention of the correlation. There was a positive correlation between BIS and EMG and it was statistically significant (R: 0.679, p<0.05). There was a strong negative correlation between BIS and SR and it was statistically significant (R: -0.959, p<0.05).

Discussion

In our study BIS and SR were determined as 0 and 100 respectively at the moment of brain death diagnosis in 12 of 20 patients, whereas BIS was determined >0 in the remainders. BIS median value was identified 0 (min-max 0-69) at the moment of brain death diagnosis.When the ROC curve analysis of BIS values was performed the AUC was found as 0.582 (0.576-0.588) which was statistically significant (p<0.05). At the same time, there was a positive correlation between BIS and EMG and it was statistically significant (R: 0.679, p<0.05). In addition, there was a strong negative correlation between BIS and SR and it was statistically significant (R: -0.959, p<0.05).

BIS monitoring is a non-invasive and easy to use method for critically ill patients in ICU. Some studies have reported that BIS monitoring can be useful to determine the timing for performing a comprehensive neurological examination, apnea test and an ancillary test in patients with head trauma and suspected brain death (12). In addition, some studies reported that BIS monitoring can be used for the brain death diagnosis in patients with severe coma admitted to ICU (10,16). Vivien et al. (10), in their prospective study, reported that 44 patients without brain death at ICU admission and who had BIS values ranging from 20 to 79 did progress to brain death and their BIS values decreased to 0. In contrast, in 17 patients with persistent electrocortical activity detected by EEG who did not progress to brain death after ICU admission, mean BIS values was over 35. Escudero et al. (17), in their study evaluated 19 patients, reported a gradual decrease in BIS values and an increase in SR with clinical deterioration. It was reported that BIS and SR were 0 and 100 consecutively in all patients with confirmed brain death diagnosis. We detected BIS and SR values as 0 and 100 respectively in 12 patients at the moment of brain death whereas BIS >0 and SR <100 values were recorded in the remainders. Vivien et al. (10) emphasized two important limitations of their study. Firstly, BIS values can drop to 0 before onset of the brain death in patients with major intracranial hypertension, secondly, significant EMG activity and cardiovascular hyperpulsatility may increase BIS values falsely. Escudero et al. (17), reported that low-frequency EMG activity may increase BIS values falsely in the absence of EEG activity, especially in brain death. Fyntanidou et al. (8), in their study including 35 patients, reported that BIS values consistently gave a value of 0 in 12 patients with brain death diagnosis, but in 23 patients, BIS values were >30 for more than 30 minutes. They emphasized that this change was not due to brainstem electrical activity, but it might be due to external factors such as nearby equipment or internal factors such as heartbeat. Mayr et al. (18) reported "tetaniform" muscle activity during EEG recording in five potential organ donors, suggesting that increased EEG activity may be due to hyperstability of the neuronal membrane caused by artificial hyperventilation in brain death patients. In our study, we recorded BIS values >0 in 8 patients with brain death diagnosis. This may be related to low EMG activity at the moment of brain death diagnosis, interference of nearby devices or heartbeat. In clinical practice, some studies suggested that EMG activity should always be considered for the interpretation of BIS values in severely comatose patients and even neuromuscular blockers may be used in some cases (10). But we did not use neuromuscular blockers during BIS monitoring. In our study, there was a positive

correlation between BIS and EMG and it was statistically significant (R: 0.679, p<0.05). Dunham et al. (12), performed a study including 27 patients, and compared BIS values of the patients with brain death and without brain death. They reported that BIS values of the patients with brain death were significantly lower. They reported that BIS value was <5 in 83% of the patients with brain death diagnosis. In the same study, they reported the sensitivity of BIS <20 as 100%, positive predictive value as 82%, negative predictive value as 100% and accuracy as 87%. Jouffroy et al. (19), prospectively evaluated 46 patients, identified that mean BIS value was 4 in 29 patients with brain death under therapeutic hypothermia and it was 0 after warming. BIS values were found to be significantly different between patients with and without brain death. The sensitivity and specificity of the BIS <30 cut-off value during the ICU stay were 96% and 82% respectively for brain death.

In our study, when ROC analysis of BIS values was performed during the brain death diagnosis, AUC was 0.582 (0.576-0.588) and it was statistically significant (p<0.05). Although AUC was as low as 0.58, it was found to be statistically significant since BIS values were measured many times (34041 repetitive BIS data) from the time of ICU admission in 20 patients with brain death. The sensitivity and specificity of ROC curve analysis for BIS were 0.752, 0.384 respectively and optimal diagnosis value was identified 1.5. While the sensitivity is 0.752, it is unacceptable that the specificity is 0.384. As the value of n was 34041 (repeated BIS values) and the confidence interval was 95% (0.576-0.588), the ROC value may be statistically significant. Although this value is an acceptable level for the validity of a diagnostic test in the field of health, it was not considered statistically significant (20).

Miao et al. (21), used BIS monitoring in 90 patients with coma, reported AUC of BIS values as 0.841 (p<0.001, 95% CI =0.751-0.931). They suggested that BIS may reflect the degree of brain injury and it may help clinicians predict brain death in patients whose BIS value <32.5. On the other hand, Dou et al. (16), evaluated 208 patients with coma, they found that AUC of BIS was <0.5 in their study. In addition, they stated that BIS values <42.5 can not differentiate vegetative state and brain death.

Conclusion

BIS is a non-invasive method and it may be used in ICU. BIS monitoring may be useful especially in patients with head trauma and GCS =3. BIS monitoring provides an information about the neurological prognosis and may be used to determine the moment of brain death. When BIS dropped to 0 in patients with brain death suspect, the neurological examination should be repeated and if it is necessary, the brain death diagnosis should be confirmed by ancillary methods such as TCD and CTA. However, EMG activity that may affect BIS values should be considered. We consider that BIS monitoring can prevent loss of time by providing to detect the moment of the brain death and so facilitate the organ transplantation process and however it can not take the place of the other ancillary methods.

Ethics

Ethics Committee Approval: Study was performed between 2016-2017 in Dokuz Eylül University (DEU) Faculty of Medicine ICU after DEU Non-Interventional Research Ethics Committee approval (decision no: 2016/19-05, date: 14.07.2016).

Informed Consent: No additional consent was obtained from the patient relatives for the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: K.A., Y.L.U., T.Ç., Concept: K.A., Y.L.U., T.Ç., P.K., A.N.G., Design: K.A., Y.L.U., T.Ç., B.E., T.M., Y.S., E.Y., B.C., U.K., P.K., A.N.G., Data Collection or Processing: K.A., Y.L.U., T.Ç., T.M., Y.S., E.Y., B.C., U.K., A.N.G., Analysis or Interpretation: K.A., Y.L.U., T.Ç., B.E., T.M., Y.S., E.Y., B.C., U.K., P.K., A.N.G., Literature Search: K.A., Y.L.U., T.Ç., B.E., T.M., Y.S., E.Y., B.C., U.K., P.K., A.N.G., Writing: K.A., Y.L.U., T.Ç., B.E., T.M., Y.S., E.Y., B.C., U.K., P.K., A.N.G.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Gardiner D, Shemie S, Manara A, Opdam H. International perspective on the diagnosis of death. Br J Anaesth 2012;108 Suppl 1:i14-28.
2. Wijdicks EFM. Brain death worldwide: accepted fact but no global consensus in diagnostic criteria. Neurology 2002;58:20-5.
3. Arsava EM, Demirkaya Ş, Dora B, Giray S, Gökçe M, Güler A, et al. Diagnostic Guidelines for Brain Death*. Turkish J Neurol 2014;20:101-4.
4. Citerio G, Murphy PG. Brain death: The European perspective. Semin Neurol 2015;35:139-44.
5. Paolin A, Manuali A, Di Paola F, Boccaletto E, Caputo P, Zanata R, et al. Reliability in diagnosis of brain death. Intensive Care Med 1995;21:657-62.
6. Misis M, Raxach JG, Molto HP, Vega SM, Rico PS. Bispectral index monitoring for early detection of brain death. Transplant Proc 2008;40:1279-81.
7. Johansen JW. Update on bispectral index monitoring, Best Pract Res Clin Anaesthesiol 2006;20:81-99.
8. Fyntanidou B, Grosomanidis V, Aidoni Z, Thoma G, Giakoumis M, Kiurzieva E, et al. Bispectral index scale variations in patients diagnosed with brain death. Transplant Proc 2012;44:2702-5.
9. Bilgili B, Montoya JC, Layon AJ, Berger AL, Kirchner HL, Gupta LK, et al. Utilizing bi-spectral index (BIS) for the monitoring of sedated adult ICU patients: a systematic review. Minerva Anestesiol 2017;83:288-301.
10. Vivien B, Paqueron X, Le Cosquer P, Langeron O, Coriat P, Riou B. Detection of brain death onset using the bispectral index in severely comatose patients. Intensive Care Med 2002;28:419-25.
11. Fàbregas N, Gambús PL, Valero R, Carrero EJ, Salvador L, Zavala E, et al. Can bispectral index monitoring predict recovery of consciousness in patients with severe brain injury? Anesthesiology 2004;101:43-51.
12. Dunham CM, Katradis DA, Williams MD. The bispectral index, a useful adjunct for the timely diagnosis of brain death in the comatose trauma patient. Am J Surg 2009;198:846-51.
13. Okuyaz C, Birbiçer H, Doruk N, Atici A. Bispectral index monitoring in confirmation of brain death in children. J Child Neurol 2006;21:799-801.
14. Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ, et al. Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition. Neurosurgery 2017;80:6-15.
15. Resmi Gazete. Sağlık Bakanlığı ve bağlı kuruluşlarının teşkilat ve görevleri hakkında kanun hükmünde kararname ile bazı kanunlarda değişiklik yapılmasına dair kanun. Kanun No. 6514. Kabul Tarihi: 02/01/2014. Erişim Linki: URL: http://www.resmigazete.gov.tr/eskiler/2014/01/20140118-1.htm. Erişim Tarihi: Ocak 21, 2020.
16. Dou L, Gao H, Lu L, Chang WX. Bispectral index in predicting the prognosis of patients with coma in intensive care unit. World J Emerg Med 2014;5:53-6.
17. Escudero D, Otero J, Muñiz G, Gonzalo JA, Calleja C, González A, et al. The Bispectral Index Scale: Its use in the detection of brain death. Transplant Proc 2005;37:3661-3.
18. Mayr N, Zeitlhofer J, Auff E, Wessely P, Deecke L. Die Bedeutung von EMG-Artefakten im isoelektrischen EEG [The significance of EMG artefacts in isoelectric EEG]. EEG EMG Z Elektroenzephalogr Elektromyogr Verwandte Geb 1990;21:56-8.
19. Jouffroy R, Lamhaut L, Guyard A, Philippe P, An K, Spaulding C, et al. Early detection of brain death using the Bispectral Index (BIS) in patients treated by extracorporeal cardiopulmonary resuscitation (E-CPR) for refractory cardiac arrest. Resuscitation 2017;120:8-13.
20. Zhou X-H, Obuchowski NA, McClish DK. Statistical Methods in Diagnostic Medicine. New York: John Wiley & Sons; 2002.
21. Miao W, Zhang Y, Li H. Bispectral index predicts deaths within 2 weeks in coma patients, a better predictor than serum neuron-specific enolase or S100 protein. J Anesth 2013;27:855-61.