Assessing the Consistency of Clinical Diagnosis and Ancillary Tests For Brain Death

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Abstract

Objective: Brain death (BD) implies the permanent absence of cerebral and brainstem functions. It should be shown that there is no blood flow in all brain regions even besides the brainstem by using the confirmatory tests. We aimed to evaluate the incompatibility to diagnosis of BD by clinical and ancillary tests (computed tomographic angiography (CTA), magnetic resonance imaging angiography (MRIA), transcranial Doppler ultrasonography (TCD-USG), electroencephalography (EEG)).

Methods: The patients admitted to our intensive care unit between 2012-2018 have been evaluated retrospectively. Twenty two patients who were assessed as BD, and additionally 12 of them had ancillary tests for BD for certain diagnosis investigated. Demographic data, causes of BD, and the follow ups were recorded for all patients.

Results: Twelve patients were diagnosed as BD. The reasons leading to BD were intracranial hemorrhage, cardiac arrest, intracranial tumours, pulmonary embolism, aneurysmal hemorrhage, menengitis, subarachnoid hemorrhage. The mean age was 40.86±15.62 years, the mean APACHE II score was 28.23±16.33. Brain death was diagnosed by clinically in 10 patients, and 12 patients evaluated by ancillary tests.

Conclusion: Brain death can be diagnosed based on clinical criteria, but in somehow confirmative tests may be necessary. Clinically diagnosing of BD is not always consistent with CTA, and procedure is needed to be repeated or other further techniques have to be used for confirmation.

Keywords: Brain death, ancillary tests, computed tomographic angiography

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Beyin ölümü için klinik tanı ve yardımcı testlerin tutarlılığı

Öz

Amaç: Beyin ölümü (BÖ), beyin ve beyin sapı işlevlerinin kalıcı yokluğunu ifade eder. Doğrulayıcı testler kullanılarak beyin sapı dışında bile tüm beyin bölgelerinde kan akışı olmadığı gösterilmelidir. BÖ tanısının uyumsuzluğunu klinik ve yardımcı testler (bilgisayarlı tomografik anjiyografi (BTA), manyetik rezonans görüntüleme anjiyografisi (MRIA), transkranial Doppler ultrasonografi (TKD-USG), elektroensefalografi (EEG)) ile değerlendirmeyi amaçladık.

Yöntemler: 2012-2018 yılları arasında yoğun bakım ünitemize başvuran hastalar retrospektif olarak değerlendirildi. BÖ için 22 hasta değerlendirildi ve ayrıca 12 tanesinde, BÖ tanısında kesin tanı için yardımcı testler yapıldı. Tüm hastalar için demografik veriler, BÖ'nün nedenleri ve takipleri kaydedildi.

Bulgular: On iki hastaya BÖ tanısı kondu. BÖ'ye neden olan nedenler intrakraniyal kanama, kardiyak arrest, intrakraniyal tümörler, pulmoner emboli, anevrizmal kanama, menenjit, subaraknoid kanama idi. Yaş ortalaması 40,86±15,62, ortalama APACHE II skoru 28,23±16,33 idi. Beyin ölümü 10 hastada klinik olarak teşhis edildi ve 12 hasta yardımcı testlerle değerlendirildi.

Sonuç: Beyin ölümü klinik kriterlere göre teşhis edilebilir, ancak bir şekilde doğrulayıcı testler gerekli olabilir. BÖ'nün klinik olarak tanısı her zaman BTA ile tutarlı değildir ve tekrarlanması için prosedür gereklidir veya başka ileri teknikler kullanılmalıdır.

Anahtar Sözcükler: Beyin ölümü, yardımcı tanı testleri, bilgisayarlı tomografik anjiyografi

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Brain death (BD) is commonly defined as the irreversible cessation of consciousness (irreversible coma), all motor responses (excluding spinal reflexes), and all brainstem functions (including respiration) as a consequence of a catastrophic brain injury [1-5]. This results from prolonged cerebral circulatory arrest and leads to hypoxia, fatigue, and eventually cellular necrosis. In 1959, Mollaret and Goulon first described this state as "coma deepassé" or irretrievable coma [6].

The diagnosis of BD is predominantly made clinically [7]. However, in the absence of a reliable examination, ancillary tests may be necessary for a timely diagnosis [8-11]. Most countries have laws regulating the diagnosis of BD and organ of organs from donors.

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However, the criteria and guidelines for the same differ from country to country [6].

Confirmatory ancillary tests demonstrate the absence of cerebral electrical activity or depict cerebral circulatory arrest. Four-vessel cerebral angiography has traditionally been considered the standard criterion for diagnoses of BD. However, its invasive nature, need for specially trained physicians, technical complexity, specialized equipment, high cost, and inconsistent availability across hospitals make it of limited use today [9, 10, 12, 13].

As a result, a number of surrogate cerebral circulatory tests have been introduced, such as nuclear medicine perfusion test, transcranial Doppler ultrasonography (TCD-USG), computed tomographic angiography (CTA), magnetic resonance imaging angiography (MRIA), perfusion computed tomography (CT), xenon CT, MR perfusion, diffusion-weighted MR imaging, and functional MR imaging [10].

Perceptions and practices regarding BD vary worldwide. Ancillary tests are not mandatory but can be used in cases of apnea, inconclusive clinical examination, or to shorten the duration of the observation period [14].

We aimed to evaluate the incompatibility of the diagnosis of BD with clinical examination and ancillary tests such as CTA, MRIA, TCD-USG, and electroencephalography (EEG).

Material and methods

After obtaining approval from the local ethics committee, 22 patients who were admitted to our intensive care unit with findings of BD between 2012 and 2018 were evaluated retrospectively. Confirmatory tests were recorded to assess the demographic data, underlying causes of BD, APACHE II scores, apnea test time, the time from the first suspicion of BD with neurological findings to time of declaration of BD.

Results

In this study, 22 patients (12 male and 10 female) were diagnosed with BD and evaluated retrospectively. The mean age was 40.86±15.62 years, and the mean APACHE II was 28.23±16.33. The reasons leading to BD in the study group were intracranial hemorrhage in 10 patients (45.45%), cardiac arrest in 3 patients (13.63%), intracranial tumor in 3 patients (13.63%), pulmonary embolism in 2 patients (9.09%), aneurysmal hemorrhage in 2 patients (9.09%), meningitis in 1 patient (4.54%), and subarachnoid hemorrhage in 1 patient (4.54%).

The apnea test time was 8.68±5.19 minutes. The time from the first suspicion of BD with neurological findings to the time of declaration of BD was 70.9±132.66 hours.

Table 1. Causes of brain death (BD)

Causes	n (%)
Intracranial hemorrhage	10 (45.45)
Cardiac arrest	3 (13.63)
Intracranial tumour	3 (13.63)
Pulmonary embolism	2 (9.09)
Aneurysmal hemorrhage	2 (9.09)
Menengitis	1 (4.54)
Subarachnoid hemorrhage	1 (4.54)

Ancillary tests (CTA, EEG, MRIA, TCD-USG) were performed on 12 patients. CTA was performed in 8 patients, and it was positively correlated with clinical examination in only 6 patients (75%). After clinical progress, 2 cases that showed negative CTA results were accepted as BD based on further CTA or on subsequent EEG. MRIA was performed in 2 patients and was found to be positive in 1 patient, while the other negative result was accepted as being compatible with BD after being reevaluated by CTA. EEG and TCD-USG were both positive in 1 patient each. BD was diagnosed clinically in 10 patients.

Discussion

According to the law in Turkey, BD is defined as the irreversible cessation of all functions of the entire brain, including the cerebrum and brainstem. Keeping in line with the recent medical achievements in organ transplantation, the diagnosis of BD is particularly important [10]. In our protocol, the clinical diagnosis of BD was made by two independent physicians (an anesthesiologist/intensivist and a neurologist/neurosurgeon) depending on the presence of deep unresponsive coma, the absence of all brainstem reflexes (dilated pupils that were non-reactive to light and trigeminal pain stimuli and absence of gag, corneal, oculocephalic and oculovestibular reflexes) and a positive apnea test. In some protocols, repeating the clinical evaluation after a 12–72 hour duration has been suggested [15]. In our study, we repeated the neurological examination twice in a 12–24 hour period after the first neurological examination.

In most countries, the apnea test is performed because it is legally required or recommended in the guidelines. Although there are many arguments about the apnea test, it is considered safe as long as adequate oxygen is provided to the patient [16]. In our study, the apnea test was performed for all suspicious BD patients as a rule.

After completing the clinical diagnosis of BD, the lack of brain function or cerebral circulation can be demonstrated using ancillary methods such as EEG, TCD-USG, and conventional angiography [17]. In Europe, there are different approaches defined for the use of ancillary tests in the diagnosis of BD [18]. Most series have shown that CTA has demonstrated high sensitivity, specificity, and validity in detecting intracranial circulatory arrest [19]. This method was described for use in BD diagnosis in 1978 and has since has benefited from advances in imaging techniques that make it quick and easy to perform [20, 21]. On the other hand, some studies have suggested that CTA is not a valid confirmatory test for cerebral circulatory arrest in BD, as it may be associated with false-positive results and lower sensitivity compared to EEG [22, 23]. In Turkey, the most frequently used ancillary test was CTA (46.5%), followed by TCD-USG (24.4%) [24]. Similarly, in our study, the most frequently used test was CTA.

Other ancillary tests used for BD diagnosis have some pitfalls. EEG is routinely used for BD diagnosis in 54% of hospitals. It was one of the first ancillary tests described to confirm the diagnosis of BD [25]. But this test has many limitations [26] such as the fact that EEG cannot be performed or is difficult to interpret in patients with hypothermia, severe metabolic disorders, drug intoxications, or hemodynamic instability. Further, TCD-USG is operator-dependent and deficient for posterior circulation [27-29].

In the literature, the most common cause of BD is intracranial hemorrhage [30]. In our study, the most common cause was intracranial hemorrhage (45.45%), and the other causes were cardiac arrest (13.63%), intracranial tumor (13.63%), pulmonary embolism (9.09%), aneurysmal hemorrhage (9.09%), meningitis (4.54%), and subarachnoid hemorrhage (4.54%).

There are different opinions in previous literature about the duration of the apnea test. In a study by Saritas et al. [24], 37.4% of the participants stated that a duration of 8–10 minutes was needed to obtain an increase of >20 mmHg in the arterial partial pressure of CO_2 from baseline till a value of >60 mmHg at the end of the test. In our study, the apnea test time was 8.68±5.19 minutes.

After the apnea test, 10 of the 22 patients were accepted as having BD by clinical examination. Ancillary tests (CTA, EEG, MRIA, TCD-USG) were performed on 12 patients. CTA was performed in 8 patients, and it was positively correlated with clinical examination in only 6 patients (75%). After clinical progress, 2 cases that showed negative CTA results were accepted as BD based on further CTA or on subsequent EEG. MRIA was performed in 2 patients and was found to be positive in 1 patient, while the other negative result was accepted as being compatible with BD after being reevaluated by CTA. EEG and TCD-USG were both positive in 1 patient each.

In nine patients, the duration between the apnea test and the ancillary test was 18.66±20.80 hours. Three patients who had negative results in the first screening (MRIA and CTA) needed a second screening to confirm the lack of cerebral circulation. In these three patients, the duration between the apnea test and the second ancillary (CTA-EEG) test was 267.33±296.42 hours.

All the 22 patients showed a positive result on the apnea test but 12 patients required ancillary tests (CTA, EEG, MRIA, TCD-USG) to confirm the diagnosis of BD. Finally, all 22 patients were confirmed as having BD.

Negative results of three ancillary tests delayed the time of declaration of BD, which further delayed organ transplantation. Moreover, the exact time of CTA in the diagnosis of BD should also be elucidated in further studies.

Our study has some limitations in that the sample size was less and that it was a single-center study.

In conclusion, any condition that causes permanent widespread brain injury can lead to BD. BD can be diagnosed based on clinical criteria, but some confirmatory tests may be necessary. Verification of the absence of cerebral circulation is crucial in the confirmation of BD diagnosis. Confirmatory tests that can be conducted radiologically are intracranial blood flow examinations which include CTA, MRIA, cerebral angiography and venography, ophthalmic artery flow examinations, and TCD-USG examinations. Legal definitions of BD vary from country to country.

Compared to other ancillary tests for BD, CTA is the most reliable, standardized, and widely accessible one and can examine the whole body, making it particularly useful in cases in which there is potential for organ harvesting.

When clinical examination for diagnosis of BD is not consistent with CTA, either the method of diagnosis should be repeated or other techniques should be employed for confirmation.

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