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Clinical Diagnosis and Ancillary Tests in Brain Death: Effects on The Organ Donation Process

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ABSTRACT

Objective: Demographic data of patients diagnosed as brain dead at our intensive care unit were evaluated along with the methods used to diagnose brain death, their effects on the timing of the diagnosis, and their effects on each family's donation decision as well as the reasons for donation refusal.

Methods: In this single-center study, data of patients diagnosed with brain death at the tertiary intensive care unit (ICU), between January 2012 and December 2018 were evaluated retrospectively.

Results: The data of a total of 110 patients diagnosed in ICU were evaluated. The BD diagnosis time was median (min-max) 24.5 hours (12-48) in the clinical evaluation group (Group I) and 20.5 hours (7-28) in the ancillary confirmatory test group (Group II). In Group I, the diagnostic time was significantly shorter in comparison with group II. Family organ donation consent could not be obtained in 61 (55.5%) of 110 cases. No significant difference was found between Groups I and II in terms of organ donation consent.The most common reasons for refusal of organ donation rejection was concern about disruption of body integrity (31.1%), not believing in brain death (24.6%), religious reasons (11.5%) and disagreement of family members (6.6%), respectively.

Conclusion: According to the results of our study, the use of the ancillary confirmatory test in the diagnosis of brain death is recommended because it shortens the duration of the diagnosis. According to the results of our study, the method of diagnosis did not affect family decisions.

Keywords: Brain death,organ donation,organ procuremen, intensive care unit

Introduction

Brain death is defined as the irreversible loss of all brain and brainstem functions in the presence of a catastrophic brain injury (1). The diagnosis of brain death is a medical and legal responsibility and must be performed both accurately and quickly. Patients diagnosed with brain death are potential donor candidates, which increases the importance of this issue given that organ transplantation is the only treatment option for patients with end-stage organ failure (2).

Although there is global consensus on the clinical diagnosis of brain death, there are significant differences in the use of ancillary confirmatory tests among countries. In Turkey, as in most other countries, ancillary tests are most commonly used when the clinical evaluation is not reliable and in the presence of confounding factors (e.g., sedative drugs, electrolyte disturbances, acid-base disorders, intoxication, or body temperature <35°C) and/or when the examination of brainstem reflexes and/or apnea tests cannot be performed (e.g., facial trauma)(3). Routine use of confirmatory tests in the diagnosis of brain death is mandatory in half of all European countries (4).

Increased demand of organ transplantation and low transplantation rates are major problems both in Turkey and the rest of the world (5). To increase the donor pool of cadavers, the possibility of brain death should not be overlooked, the diagnosis should be made as soon as possible, optimization of organ viability should be achieved, and the rate of rejection of family organ donations should be reduced.

Even after the diagnosis of brain death is made, family refusal is an obstacle to organ donation. Although donation refusal may be associated with cultural and religious beliefs, the main factor affecting a family's decision is whether they understand the meaning of brain death.

Aim

Demographic data of patients diagnosed as brain dead at our tertiary intensive care unit were examined along with the methods used to diagnose brain death, their effects on the timing of the diagnosis, and their effects on each family's donation decision as well as the reasons for donation refusal.

Methods

In this single-center study, data of patients diagnosed with brain death at the tertiary intensive care unit (ICU), between January 2012 and December 2018 were evaluated retrospectively.

Data collection

Patient data were obtained from the hospital data network and from the records of the national transplantation, dialysis, and monitoring systems data network through the organ transplant coordinator. All patients diagnosed with brain death in our ICU were included in this study. Patients who were diagnosed with brain death at ICU admission and patients lacking sufficient data to perform a statistical analysis were excluded from the study.

There were two groups in our study: the clinical evaluation group and the ancillary confirmatory test group.

Group I: Clinical evaluation group

In this group, the diagnosis of brain death was made according to criteria published in the Official Gazette of the Ministry of Health (dated 1 February 2012). An irreversible coma, absence of brainstem reflexes, and positive apnea test were confirmed by two specialist physicians (a neurosurgeon or neurologist and an anesthesiologist or intensive care specialist), and a second neurological examination was performed after a waiting period to confirm the irreversibility of the coma and lack of brainstem reflexes. An etiological examination and radiological imaging of the brain to confirm the cause of the coma were performed in all patients with clinically diagnosed brain death.

Group II: Ancillary confirmatory test group

Clinical examination supported by ancillary confirmatory testing for brain death:

After all preconditions were met, the diagnosis of brain death was clinically initiated with apnea test positivity and a neurological examination. A diagnosis of brain death was verified after confirming the absence of cerebral blood circulation by computed tomography angiography (CTA) or by demonstration of the hollow skull phenomenon with radionuclide cerebral perfusion scintigraphy (RCPS).

Diagnosis of brain death only by ancillary confirmatory testing:

An ancillary confirmatory test to evaluate brain blood circulation is mandatory in accordance with our national laws in cases where preconditions for the diagnosis of brain death are not met or a clinical evaluation cannot be completed (6). At our clinic, the diagnosis of brain death was confirmed in this patient group by the absence of cerebral blood circulation with CTA or the presence of the hollow skull phenomenon with RCPS.

Statistical analysis

In this study, the Shapiro-Wilk normality test was used to examine differences between the groups in terms of numerical variables. As descriptive statistics, the mean ± standard deviation or median (minimum – maximum), based on assumptions for numerical variables, and the categorical variable frequency (*n*) and percentage (%) are given.

The Mann-Whitney U test was used to examine the significance of differences between the two groups in terms of numerical variables. Pearson's chi-square test was used to analyze categorical variables. In all analyses, the probability of a type I error was taken as 0.05. All analyses were performed using IBM SPSS v22 software (IBM Corp., Armonk, NY, USA).

Results

Data from 116 patients diagnosed with brain death in our ICU were evaluated. Six patients were excluded due to a lack of data. Sixty-three of the cases (57.3%) were male and the median age was 50.3 ± 16.5 years. The most common causes of brain death were aneurysmal subarachnoid hemorrhage (*n* = 39, 35.5%), traumatic brain injury (*n* = 22, 20%), intracerebral hemorrhage (*n* = 17, 15.4%), ischemic stroke (*n* = 15, 13.6%), anoxic encephalopathy (*n* = 6, 5.5%), intoxication (*n* = 4, 3.6%), and brain tumor (*n* = 7, 6.4%). The median length of stay in the ICU (minimum – maximum) was 5 (2 – 26) days (Table 1).

Table 1. Demographic data of patients with brain death in anesthesia intensive care unit : January 2012 and December 2018

Variables	All Patients
Number of patients diagnosed with brain death	n=110
Gender: Female / Male n (%)	47 (42.7%) / 63(57.3%)
Age, years (mean±SD)	50.32±16.47
Causes of death	
- Aneurysmal subarachnoid haemorrhage	39 (35.5%)
- Traumatic brain injury	22 (20 %)
- Intracerebral hemorrhage	17 (15.4%)
- Ischaemic stroke	15 (13.6%)
- Anoxic encephalopathy	6 (5.5%)
- Intoxication	4 (3.6%)
- Brain tumor	7 (6.4%)
Length of stay in the ICU(day) Median (min-max)	5 (2-26)

Data are reported as number (N) (%), mean or median (IQR -Inter Quartile Range)
BD: Brain Death; ICU: Intensive Care Unit

According to the brain death diagnosis method, 25 (22.7%) of the cases were classified as Clinical evaluation group (Group I) and 85 cases as Ancillary confirmatory test group (Group II). Brain death of 59 of the cases in Group II was diagnosed with clinical diagnosis supported by ancillary confirmatory test. However, in 26 of the cases in the same group, brain death was diagnosed only by ancillary confirmatory test as the clinical diagnosis was not completed due to confounding factors (Table 2).

Table 2. Characteristics of brain death diagnosis approach

Variables	Case Number
Diagnostic method of brain death n (%)	
- Clinical evaluation group (Group I)	25 (22.7%)
- Ancillary confirmatory test group (Group II)	85(77.3%)
Clinical examination supported by ancillary confirmatory test for BD diagnosis	59 (53.6%)
Diagnoses of brain death only by ancillary confirmatory test	26 (23.7%)
Causes of failure to complete clinical evaluation (n (%)	n=26
- Apnoea test failure	16 (61.5%)
- Intoxication	4 (15.4%)
- Sedative infusion	3 (11.5%)
- Facial trauma	2 (7.7%)
- y, hypernatremia (170 mmol/L)	1 (3.9%)
Ancillary confirmatory tests n (%)	85
CTA confirmed BD	63 (74.1%)
RCPS confirmed BD	22 (25.9%)

Data are reported as n (%) n: number, BD: Brain Death; CTA: Computed Tomography Angiography; RCPS: Radionuclide Cerebral Perfusion Scintigraphy

The reasons for the incomplete clinical evaluation were apnea test failure in 16 (61.5%) cases, intoxication in 4 cases (15.4%), sedative infusion in 3 cases (11.5%), facial trauma in 2 cases (7.7%), and hypernatremia in 1 case (3.9%). (Table 2)

The ancillary test preference was CTA in 63 cases (74.1%) and RCPS in 22 (25.9%) cases. (Table 2)

The median (minimum – maximum) time from clinical suspicion to diagnosis of brain death was 24.5 (12 – 48) h in the clinical evaluation group (Group I) and 20.5 (7 – 28) h in the ancillary confirmatory test group (Group II). The time until diagnosis was significantly shorter in Group II than in Group I ($p < 0.001$) (Table 3).

Table 3. Brain death diagnosis approach and time taken

	Clinical evaluation group (Group I)	Ancillary confirmatory test group (Group II)	p
Time to diagnose BD (hour) Median (min-max)	24.5 (12-48)	20.5(7-28)	<0.001[a]

a: Mann-Whitney U. Test,statistical significance: p <0.001. BD: brain death

The effects of brain death diagnosis on family organ donation were evaluated. No significant difference was found between Groups I and II (Table 4). Family consent was obtained for organ donation in 49 (44.5%) of 110 cases, and these cases were accepted as donors. The organs of 42 of the cases were transferred to the recipients. The remaining seven patients were not suitable as organ transplant donors because four had a diagnosis of brain tumor, two had no organs healthy enough for transplantation, and one had a history of organ transplantation (Table 5). Family organ donation consent could not be obtained in 61 (55.5%) of 110 cases, the reasons for which were as follows: concern about disruption of body integrity (n = 19, 31.1%), not believing in brain death (n = 15, 24.6%), religious reasons (n = 7, 11.5%), and lack of consensus among family members (n = 4, 6.6%). Data regarding the reasons for family rejection could not be obtained in 16 (26.2%) cases (Table 5).

Table 5. Family decision on organ donation and causes of family refusal of organ donation

Family decision on organ donation	
- Family approval	49 (44.5%)
- Family rejection	61 (55.5%)
Donor n (%)	49(44.5%)
- Organ procurement available from donor	42 (85.7%)
- Organ procurement not available from donor	7(14.3%)
Causes of family refusal of organ donation	
- Disfiguration of the body	19 (31.1%)
- Denial and rejection of BD	15 (24.6%)
- Religious beliefs	7 (11.5%)
- Lack of consensus among family members	4 (6.6%)
- Unknown	16 (26.2%)

Data are reported as n (%) n: number,

Discussion

According to the results of our study, although the use of an ancillary confirmatory test in the diagnosis of brain death shortens the diagnosis time, it does not affect the organ donation rate. The most common reasons for refusing to donate by families encountered in our study were disruption of body integrity, lack of belief in the concept of brain death, religious beliefs, and disagreements between family members.

End-stage organ failure is associated with increased mortality and morbidity in addition to increased health care costs. Organ transplantation is the only treatment that improves survival and the quality of life in patients with end-stage organ failure. However, waiting lists for suitable organs continue to grow worldwide due to the discrepancy between demand and availability of organ donors. To minimize donor loss, clinicians should not delay the diagnosis of brain death and attempt to reduce the reasons for family rejection, which are important steps in the organ donation process (7,8).

Method and time of brain death diagnosis

Despite different approaches worldwide, the diagnosis of brain death is mainly based on clinical examination (2). Many

Table 4. Determination of the effect of BD diagnosis method on family organ donation

		Family approval	Family Rejection	p
Diagnostic Method of BD	Clinical evaluation group (Group I)	10	15	0.475[a]
	Ancillary confirmatory test group (Group II)	39	46	

a: Pearson Chi-Square Test **BD**: Brain Death

confounding factors make it impossible to clinically detect death; therefore, the use of supplementary tests is mandatory. Considering significant errors and obvious instability of the protocols described in the literature in the diagnosis of brain death, ancillary tests provide protection against misdiagnosis (9).

The care of potential donors in the ICU is crucial for the protection of organs. Hemodynamic instability, hormonal imbalances, and immune system activation may cause progressive dysfunction of all organs in potential donors (10). Prolongation of the duration of brain death diagnosis, documentation, and organ extraction procedures will lead to organ loss (11). As brain death is a catastrophic event and reducing the diagnostic time increases transplant organ viability, the diagnosis of brain death within the shortest time possible is the main step in the organ donation process.

Lustbader et al. (12) reported that a second neurological evaluation prolongs the diagnostic range and consequently increases the rate of organ loss. In another study examining the effects of time management in cases of brain death, a shorter time interval between diagnosis and declaration of brain death was shown to increase the number of organs transplanted per donor (13). In the present study, we found that the use of an ancillary test significantly shortened the duration of diagnosis ($p < 0.001$). Considering the negative effects of prolonged diagnostic time in the process of organ donation, we suggest that the use of ancillary confirmatory tests will be beneficial in terms of optimizing organ viability by shortening the time of diagnosis.

Determination of the effects of family organ donation decision

We initially hypothesized that demonstrating the existence of brain death through confirmatory tests would allow the patients' relatives to understand the concept of brain death and thus increase the organ donation rate. However, our analysis showed no significant relationship between the diagnostic method used and the organ donation rate.

Soldatos et al. (14) reported that an ancillary confirmatory test provided greater understanding and satisfaction regarding brain death to the families. However, similar to our study, there was no statistically significant effect on organ donation rate.

The use of ancillary tests may increase understanding of and satisfaction with the concept of brain death, but the decision regarding organ donation is affected by many factors. A number of studies conducted in different ethnic groups and countries showed that disturbance of body integrity (15), failure to understand or accept the concept of brain death (16), wishes of the deceased (17), disregarding the emotional needs of parents and providing insufficient information (18), time of notification of brain death (11), age, sex, and income levels of family members and religious or cultural reasons (19) are important factors affecting organ donation decisions.

Causes of Family Refusal of Organ Donation

Relationship between cultural/religious beliefs and family approval of organ donation

The religious beliefs and social and cultural status of the families have been reported to be the main factors influencing death perception and organ donation.

According to the results of our study, concern for body integrity was found to be the most common cause of organ donation refusal by the families. Even in communities with different cultures and religions, the idea of interfering with a body (i.e., cutting and destroying its integrity) is disturbing and affects organ donation decisions. Wheeler et al.(20) conducted a study among three groups from different cultures and ethnicities and reported that participants from different groups had similar concerns about life after death, fear of harming the dead person, and preserving the integrity of the deceased.

In our study, religious beliefs were another cause of refusal of organ donation by the families. In a review of 18 studies, Irwing et al.(15) reported that religious beliefs could increase organ donation by encouraging altruism or could prevent organ donation due to fear of interfering with death and the provisions of God.

In a survey conducted in 1991, Bilgel et al.(19) evaluated the attitudes of people toward organ donation. The reasons for rejecting organ donation were, in decreasing order, fear of disfiguring the body, religious beliefs, no reason, and belief in an afterlife. Attitudes toward organ donation were found to be related to level of education, age, sex, and socioeconomic status. They repeated the same study after 12 years, and found that the rate of religious beliefs as reasons for rejection had decreased, while the ratio of those who did not have any reasons had increased. However, they did not find any difference in total organ donation rates. They stated that the decision of the High Council of Religious Affairs on 6 March 1980 indicating that organ transplantation was legal had affected the rates and that the decision had successfully reached the masses (21).

Concerns about the deterioration of body integrity may be related to long-held beliefs, such as the illusion that life continues, the desire of the deceased to remain at peace, or to the feeling of disrespect to the body, as much as to religious beliefs.

While public campaigns generally help to promote organ donation, community education may be more efficient at challenging cultural attitudes and beliefs (22,23).

Understanding the concept of brain death and the relationship with family approval

The continuation of the heartbeat and breathing of the donor candidate with the help of machines makes it difficult for family members to accept that the patient has died. The apparent vitality of the body creates the misimpression of life. Many studies have shown that families' lack of information about brain death and the definition of brain death continue even in those who provide consent for organ donation (16). It is difficult for health care personnel to explain to the family that the patient's brain has undergone irreversible injury and that physical death will occur soon. In such cases, a satisfactory explanation of brain death may help the family to accept death and make the decision of organ donation easier (14,16,23,24).

In this context, the development of protocols for health teams to communicate with the families of potential organ donors will be useful to increase the rates of organ donation (16). Information forms regarding brain death should be developed, and informative leaflets should be provided to all family members on their first visit to the ICU (23,25).

In addition, ensuring that the families of donor candidates believe that all possible treatments were applied and that they are well informed by the physicians about the development of pathologies and brain death and understand the concept of brain death represent important steps in increasing organ donation rates.

Another reason for refusal in our study was the lack of consensus among family members, as in four (6.6%) cases. A declaration by an individual that they want to be an organ donor on their death and stating so in their will is another important factor to increase organ donation rates. Encouraging individuals to declare that they wish to donate their organs will enable families to make positive decisions about donations (17).

Conclusion

Our results show that the use of an ancillary confirmatory test in the diagnosis of brain death reduces the duration of diagnosis, which is important for donor care and organ health. However, performing these tests is not associated with an increase in family organ donation rate. The most common reasons for the refusal of donation by the families encountered in our study were concerns about the disruption of body integrity, lack of belief in the concept of brain death, religious beliefs, and disagreement among family members. Increasing the availability of organs for transplantation by expanding the donor pool is essential to counter the growing list of waiting patients.

Informed Consent: Due to the retrospective design of the study, informed consent was not taken.

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