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Original Article ANESTHESIOLOGY & REANIMATION

Evaluation of patients diagnosed with brain death in the intensive care unit: 10 years of tertiary center experience in Istanbul

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ABSTRACT

OBJECTIVE: Early and accurate diagnosis of brain death in intensive care units (ICU) is essential for organ transplantation. This study aimed to evaluate the cases diagnosed with brain death in the ICU of a tertiary center in Istanbul.

METHODS: The cases diagnosed as brain death in the ICU during the ten years between January 2013 and September 2022 were evaluated retrospectively. The demographic characteristics of the patients, the diagnosis of hospitalization in the ICU, the time from arrival to the ICU until the diagnosis of brain death, the somatic survival time after the diagnosis of brain death, the acceptance rate of organ donation by the families and the organs removed were evaluated.

RESULTS: A total of 44 patients were diagnosed with brain death. The mean age of the cases was 39.7±17.4 years, and 63% were male. The most common hospitalization diagnosis was intracranial hemorrhage (81.8%). Traffic accidents, hypertensive and aneurysm-related hemorrhages, gunshot wounds, and falls from height were the most common causes of intracranial hemorrhage. Patients were admitted to the ICU most frequently from the emergency department (54%). The mean time to brain death was 7.9±6.2 days, and the somatic survival time was 1.9±1.9 days in patients who did not receive organ transplantation. While the apnea test was positive in 91% of the cases, the apnea test could not be completed in 9% of the cases. While relatives of 7% (n=3) of the cases accepted organ donation, a patient was not allowed to be an organ donor for medical reasons. Organ transplantation was performed in two patients (5%).

CONCLUSION: As in the whole world, getting treatment as soon as possible for the patients waiting on the organ transplant list in Turkiye by increasing the number of organs to be obtained from cadavers. In cases with suspected brain death in the ICU, diagnosing brain death as soon as possible and conducting family interviews with trained organ transplant coordinators will increase the number of cadaver donors. However, we think policies should be developed to ensure that society is informed and encouraged about brain death and organ donation.

Keywords: Brain death; cadaver; intensive care unit; organ donation; transplantation.

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Brain death is the irreversible loss of all activities of the brain, brainstem, and cerebellum, the part of the central nervous system that remains inside the skull. The three main findings of the clinical diagnosis of brain death are irreversible coma, brainstem areflexia, and positive apnea test [1]. According to the latest regulation published in Turkiye, a diagnosis of brain death can be made with the unanimous consent of 2 specialists, one of whom is a Neurology or Neurosurgery specialist, and the other is an Intensive Care or Anesthesiology and Reanimation Specialist [2].

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The increasing number of patients waiting for organ failure and the developments in transplantation have made organ transplantation from a cadaver; therefore, brain death and donor care are essential. In intensive care units (ICU), the diagnosis of brain death should be made early and accurately, and possible donor organ care should be done meticulously. However, it is essential for organ transplantation to meticulously maintain the transplantation processes of the organs by informing the families and obtaining their consent from a staff competent in brain death and organ transplantation.

This study aimed to evaluate the characteristics of brain death cases diagnosed in the ICU of a tertiary center in Istanbul over ten years, their families' decisions about organ donation, and the transplanted organs.

MATERIALS AND METHODS

Istanbul Kanuni Sultan Suleyman Training and Research Hospital (date: 12.10.2022 number: 206) Clinical Research Ethics Committee approved this retrospective cross-sectional study. The study was started following the principles of the Declaration of Helsinki. Patients diagnosed with brain death in the ten years (January 2013-September 2022) from the establishment of Istanbul Kanuni Sultan Suleyman Training and Research Hospital Intensive Care Unit (ICU) to this time were evaluated through brain death follow-up forms and the hospital information system.

At our hospital's ICU, patients are followed up and treated by specialists and assistant physicians working in the Anesthesiology and Reanimation Clinic. ICU, which started serving four beds at our hospital's establishment, has reached 50 beds in 10 years. In this descriptive study, the sample size was not chosen, and all cases diagnosed with brain death in 10 years were included.

Demographic characteristics of the patients, diagnosis of admission to the ICU, units they were admitted to ICU, comorbid diseases, time from access to the ICU until the diagnosis of brain death, somatic survival times after the diagnosis of brain death, tests in the diagnosis of brain death and organ donation acceptance/rejection rates of families removed organs were evaluated.

Statistical Analysis

SPSS 29.0 program (SPSS Inc., Chicago, USA) was used to analyze the data. The descriptive statistics of the study are expressed as mean±standard deviation and range of distribution for quantitative data and frequency and percentage for qualitative data.

Highlight key points

- Although the rate of organ donation is reported to be between 30-70% in international studies, in our study, organ transplantation were performed in 5% of cases of brain death.
- The most common hospitalization diagnosis of cases with brain death is intracranial hemorrhages.

  Although the rate of brain death was higher in males, all patients who accepted organ donation were female.
- The mean time from admission to the intensive care unit to the diagnosis of brain death was 7.9 days, and the mean somatic survival of the patients who did not accept organ donation was 1.9 days.

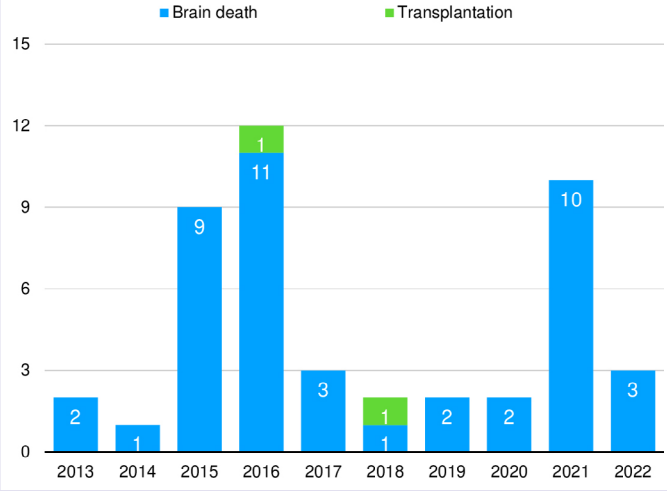

Figure 1. Number of brain death and organ transplants by year.

RESULTS

During the ten years between January 2013 and September 2022, 44 patients were diagnosed with brain death in the adult ICU of our hospital (Fig. 1). The patients' ages ranged from 7 to 73 years, with a mean age of 39.7±17.4 years. 63% (n=28) of the patients were male (Table 1). The most common diagnosis (81.8%, n=36) in which brain death cases were admitted to the ICU was intracranial hemorrhage (intracerebral, subarachnoid, subdural, and epidural hematoma). Cerebral infarction (6.8%, n=3), traumatic brain injury (4.5% n=2), postpartum hemorrhage, and septic shock (4.5%, n=2) were the other most common hospitalization diagnoses. When the causes of intracranial bleeding are examined, traffic accidents, hypertensive bleeding, bleeding due to aneurysms, gunshot wounds, and falls from height are the most common causes. There were two cases aged 7 and 9 years in the pediatric age

Table 1. Demographic data of patients, distribution of some clinical and laboratory characteristics

	All population (n=44)
Age (years)	39.7±17.4 (7–73)
Gender, (%)	
Female	36.4
Male	63.6
Comorbity, (%)	40.9
Operation, (%)	43.2
Duration of ICU (days)	9.6±6.5 (1–32)
Apnea test, (%)	
Positive	90.9
Could not complete	9.1
Diabetes insipidus, (%)	43.1
Hypotension, (%)	100
Organ donation, (%)	4.5
Brain death time (days)	7.9±6.2 (1–31)
Somatic survival time (days)	1.9±1.9 (0–9)
Blood group, (%)	
A +	36.4
B +	31.8
AB +	11.3

Values are the number of patients (n), percentage, mean±standard deviation (minimum–maximum). ICU: Intensive care unit.

Table 2. Admission to ICU for brain death cases

Diagnosis	n=44
Intracranial hemorrhage (intracerebral, subarachnoid, subdural, and epidural hemorrhage) (%)	81.8
Cerebral infarction (%)	6.8
Traumatic brain injury (%)	4.5
Postpartum hemorrhage (%)	4.5
Brain malignancy (%)	2.3

Values are expressed as the number of patients (n) and percentage.

Table 3. Units where brain death cases are admitted to the ICU

	All population n=44
Emergency (%)	54.5
Post-emergency operating room (%)	43.2
Inpatient unit (%)	2.3

Values are expressed as the number of patients (n) and percentage.

group. One pediatric patient was diagnosed with intracranial hemorrhage due to a brain tumor, and the other had traumatic brain injury due to a gunshot injury (Table 2).

Forty-one percent of the patients had at least one comorbid disease. The most common comorbid disease (27%, n=12) was hypertension. While 54% of the patients (n=24) were hospitalized directly from the emergency department to the ICU, 43.2% (n=19) were admitted to the postoperative ICU. Only one patient was admitted to our ICU with the diagnosis of cerebral infarction from an external center (Table 3). The mean duration of brain death was 7.9±6.2 (1–31) days in the cases, and the somatic survival time in the cases that did not receive organ transplantation was 1.9±1.9 (0–9) days. The duration of stay in the ICU was 9.6±6.5 (1–32) days. An apnea test was performed in all cases. In addition, all patients underwent cerebral CT (computerized tomography) angiography, one of the supportive tests. While the apnea test was positive in 90.9% (n=40) of the cases, the apnea test could not be completed in 9.1% (n=4) due to hemodynamic deterioration. The most common blood groups were A Rh(+) in 36% (n=16) of the cases, B Rh(+) in 32% (n=14) and AB Rh (+) in 11.3% (Table 1).

It was observed that 6.8% (n=3) of the cases were foreign nationals. The families of 6.8% (n=3) of the cases accepted organ donation. Since the scientific committee found it unacceptable for a patient to be an organ donor for medical reasons, they did not allow organ transplantation. Organ transplantation was not allowed because the scientific committee found it unacceptable for a patient to be an organ donor for medical reasons. Two kidneys, liver, and cornea were removed from donor 1 (51-years-old, female). Two kidneys, liver, and heart valves were removed from donor 2 (53-years-old female). Diabetes insipidus and hypernatremia were observed during follow-up in 43% (n=19) of brain death cases. Hypotension was observed in all cases, and the vasopressor agent was started.

DISCUSSION

Diseases that can only be treated with organ or tissue transplantation are significant health problems in Turkiye and worldwide. Organ transplants are made from living donors or cadavers. The heart, pancreas, lung, small intestine, and cornea are organs that can only be obtained from cadavers [3]. Since organ harvesting from a living

person may put the donor at risk in terms of health, cadaveric organ transplants should become widespread in Turkiye and developed countries. Although cadavers are the most crucial source of organ supply, the biggest obstacle to organ transplantation worldwide is the scarcity of cadaver-derived organs. The reasons for this may be the loss of potential donors without recognition, the failure of families to be allowed to donate organs or their refusal to grant, and the improper medical management of potential donors. In Europe, 80% of all organ donations come from cadavers.

On the other hand, 75% of organ donations are made from living donors and only 25% from cadavers in Turkiye [4]. Turkiye was among the countries with the highest organ donation rates in organ transplantation from living people in the world, with 52 ppm (per million people) in 2018 [4]. In our study, 44 cases were diagnosed with brain death in the ten years between 2013–2022. While the relatives of three patients accepted organ donation, the scientific committee did not allow one patient to be a donor for medical reasons. The literature has reported that the kidney and liver are the most frequently transplanted organs [5]. In our study, four kidneys, two livers, a cornea, and heart valves were taken from two patients to be transplanted into other patients.

Organ donation rates in a country are expressed as ppm (per million people). It refers to organ donation per million people. Turkiye has one of the lowest organ donation rates among all European countries, with 2.2 ppm, compared to 15–20 ppm in other European countries [4]. In studies from Turkiye, the organ donation rates of families have been reported to be 10–34% [4, 6, 7]. Jansen et al. [8] reported the organ donation rate of families as 30–40% in their multicenter studies, while the organ donation rate was reported as 70% in another study [9]. In our study, only 7% of the families (n=3) consented to organ donation. In comparison, organ transplantation was performed in 5% of the cases (n=2). Escudero et al. [9] reported that social structure, religious beliefs, and potential donor age were effective in organ donation. A study from Turkiye stated that the most common reason for the rejection of organ donation was religious reasons [10]. For organs to be harvested in cases of brain death in Turkiye, it is sufficient to state in an official or written will that they donated their organs for treatment, diagnosis, and scientific purposes while alive [2]. Even if there is an organ donation card, it is prioritized to obtain the families' consent to avoid family disputes. It is known that interviewing an expert and experienced person is adequate for families to approve organ donation. In our hospital, brain death is declared to the relatives of the patients by the Anesthesiology & Reanimation and Intensive Care specialists in the ICU. After the medical death is reported to the patient's relatives, the organ donation coordinator informs the relatives of the patient and discusses the issue of organ donation.

In the literature, there are different opinions about the hospitalization diagnoses of brain death cases. Boran et al. [10] hypoxic brain after cardiopulmonary resuscitation, Battal et al. [11] traumatic brain injury, Akbas et al. [12] reported ischemic stroke, and Karan et al. [13] said that intracranial hemorrhage was the most common cause of brain death. In a multicenter study from Spain, intracranial hemorrhage was shown as the most common cause of brain death [9]. In our research, the most common cause of brain death (82%) was intracranial hemorrhage. Considering the etiology, traffic accidents, bleeding due to aneurysms, hypertensive hemorrhages, gunshot injuries, and falls from a height are the most common causes. Cerebral infarction and traumatic brain injuries were the other most common indications for hospitalization.

Studies from Turkiye have reported that the diagnosis of brain death is more common in males [2–4, 10–13]. In a study from Iran [14], the rate of men was higher, while in a study from South Korea [15], more cases of brain death were reported in women. In our research, the brain death rate was higher in males (64% vs. 36%), which is consistent with the literature. However, in our study, all of the cases (n=3) whose families accepted organ donation were women. Akbas et al. [12] reported the mean age of brain death cases as 62±14. Ozkan Kuscu et al. [2] said that the mean age of the patients whose families accepted organ donation was significantly lower than that of those who did not (35±11 vs. 57±21). Boran et al. [10] also reported that the mean age of patients whose families accepted organ donation was lower than those who did not, although it was not significant. Since only the relatives of three patients accepted organ donation in our study, no statistical comparison was made between those who accepted and those who did not, due to the small sample size. However, unlike the literature, the mean age (38, 51, and 53 years) of the patients who were accepted for organ donation was above the general average (47 vs. 39 years).

The hospital units to which brain death cases first applied and the time spent there are essential for early diagnosis. Studies from Turkiye reported that 63–71% of brain death cases were admitted to ICUs from the emergency

services most frequently [1, 2, 5]. In our study, following the literature, the highest rate of patients (55%) was hospitalized from the emergency department to the ICU.

The times between clinical suspicion of brain death and confirmation of the diagnosis varied significantly between studies. When brain death is suspected, Akbas et al. [12] reported one day, Karasu et al. [6] reported 3 days and Yeniocak et al. [4] reported 5.1 days. In two studies of pediatric cases, Tsai et al. [16] reported 6.6 days, and Ozmert et al. [7] said 8.2 days. Yazar et al. [3] reported the time from ICU follow-up to diagnosis as six days in brain death cases. In our study, the mean time from ICU admission to the diagnosis of brain death was 7.9 days. In a retrospective study, we think it is impossible to determine the exact time between the suspicion of brain death and the diagnosis. Therefore, in our study, we specified the time between ICU admission and the diagnosis of brain death.

A positive apnea test is one of the three main findings of the clinical diagnosis of brain death. Before starting the test, the patient is ventilated with 100% oxygen for 5–10 minutes. When the test is activated, the patient is separated from the mechanical ventilator for 8–10 minutes, and 6–8 L/min oxygen support is provided through the intubation tube or tracheostomy cannula. An apnea test is considered positive if there is no spontaneous breathing and $PaCO_2$ in arterial blood gas is greater than 60 mmHg or an increase of 20 mmHg from baseline. Desaturation, hypotension, cardiac arrhythmia, and arrests may be observed during the test. In this case, the test is terminated, and the patient should be ventilated with 100% oxygen.

The test is repeated when suitable conditions are met. Supportive tests that evaluate cerebral blood flow are applied if the same situation is observed again. Studies from Turkiye reported that apnea tests could not be performed in 10–21.7% of the cases, and additional tests evaluating cerebral blood flow were needed [1, 2, 11]. In our study, in some cases, the apnea test was found to be positive in the second trial. In 9% of the cases (n=4), the apnea test could not be completed despite two attempts. Cerebral blood flow were evaluated in all of the patients in our study. In these four cases, whose apnea test could not be completed and who were clinically thought to be brain dead, the diagnosis was made with additional tests.

Until 2014, a diagnosis of brain death was made by a team of Neurology, Neurosurgery, Cardiology, and Anesthesiology Reanimation specialists within the framework of the law in force in Turkiye [1]. With the revision made in 2014, the diagnosis of brain death started with the decision of two physicians, one of whom is an Anesthesiology and Reanimation or Intensive Care Specialist, and the other is a Neurology and Neurosurgery specialist [2]. In our study, four branch specialists were found in all brain death cases (n=3) in 2014 and before. After 2015, 41 cases were diagnosed with brain death. Brain death was diagnosed by an Anesthesiology and Reanimation Neurology specialist in 24% of patients (n=10) and by an Anesthesiology and Reanimation and Neurosurgery specialist in 76% of brain death cases (n=31).

Hypotension, diabetes insipidus (DI), and electrolyte disturbances are frequently seen in patients with brain death. In the literature, hypotension has been reported in 74% to 96% of the cases [11, 17]. Akbas et al. [12] said that DI developed in 78% of brain death cases, and Youn et al. [18] in 87%. While hypotension was observed in all patients in our study, DI and hypernatremia were observed in 43% (n=19).

The time between confirmation of a diagnosis of brain death and termination of respiratory and circulatory support, known as somatic survival, differed between studies. In studies, the mean somatic survival time is between 2.5 and 6.9 days [3, 16, 19]. Escudero et al. [9] stated that all life support treatments were withdrawn in non-donor cases after the diagnosis of brain death. In our study, the mean somatic survival time after brain death was found to be 1.9±1.9 days. Although we do not routinely implement a protocol such as discontinuation of supportive treatments after the diagnosis of brain death in the ICU, the somatic survival time of the cases was shorter than the literature.

The limitations of our study are that it is retrospective, single-center, and includes a small number of cases.

Conclusion

As a result, they are treating patients waiting on the organ transplant list in Turkiye, as in the world, it is possible by increasing the number of cadaver-derived organs. In cases with suspected brain death in the ICU, diagnosing brain death as soon as possible and conducting family interviews with trained organ transplant coordinators will increase the number of cadaver donors. However, we think policies should be developed to ensure that society is informed and encouraged about brain death and organ donation. We believe that cadaveric donor loss can be attributed to identifying cadaveric donors and training on the national organ donation system.

Ethics Committee Approval: The Kanuni Sultan Suleyman Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 12.10.2022, number: 206).

Authorship Contributions: Concept – KA; Design – KA; Supervision – KA, ASS; Fundings – KA, ASS; Materials – KA; Data collection and/or processing – KA; Analysis and/or interpretation – KA, ASS; Literature review – KA, ASS; Writing – KA; Critical review – KA, ASS.

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