

# Our Five Years' Experience on the Patients with Brain Death Diagnosis: Two Centered Retrospective Study

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## ABSTRACT

Brain death (BD) diagnosis is a clinical diagnosis, but in many countries, other confirmatory tests are obligatory. The study was aimed to investigate the clinical effects of the current process of BD in Turkey.

This study was performed retrospectively by evaluating BD-diagnosed patients' files and computer records in the Van Yuzuncu Yil University Hospital's Anesthesiology Intensive Care Unit (ICU) and in a Private Istanbul Hospital's general ICU. This study was conducted between 2012 and 2017 in Turkey.

Of the 57 patients included in the study, 63.2% were male (n = 36), and 36.8% were female (n = 21). The most common causes of hospital admissions were cerebral hemorrhage (38.6%; n = 22) and trauma (36.8%; n = 21). Of the patients who accepted organ transplantation, 80% (n = 4) were diagnosed at an average of 60 hours (min 24, max 120). The rates of using imaging methods in the clinical diagnosis of BD were as follows: 75.4% (n = 43) for Computerized Tomography Angiography (CTA), 17.6% (n = 10) for Magnetic Resonance Angiography (MRA), and 7% (n = 4) for Transcranial Doppler (TD) Ultrasonography. Of the patients, 8.78% (n = 5) were used as donors.

Studies in the literature have indicated that the short duration of BD diagnosis will lead to an increase in organ donation acceptance rates. This study found that the diagnosis time was longer than presented in the literature and that CTA was the most commonly used imaging modality in addition to the apnea test.

**Key Words:** Brain death diagnosis, organ donation, intensive care unit

## Introduction

In 2017, Turkey had the highest live organ donation ratios per million people (PMP; 47.49%) worldwide. For organ donations from cadavers, Turkey was forty-first in the world, with a rate of 7.06% (1). The organ transplantations from live donors have some potential risks for donors. Therefore transplantations from cadavers are preferred primarily.

The potential risks of organ transplants from live donors indicate the importance of transplantations from cadavers (2). However the transplantations from cadavers are insufficient to meet the needs for organs, and even marginal donors have to be used (3). In Turkey, approximately 30,000 people are waiting for organ transplantation.

For organ transplantation, the ideal situation is transplantation from cadavers to live patients. However, organ donation rates from cadavers are not at sufficient levels in Turkey (4). The most important source of organ supply for transplantation, therefore, is the cases of patients with brain death (BD) in intensive care units (ICUs). An early diagnosis of BD

prevents unnecessary treatments and raises transplantation success rates (5,6). However, the knowledge of BD found in the literature does not suggest supportive tests when neurological examinations and apnea tests are performed. It does suggest supportive tests when neurological examinations are not performed, as well as in pediatric age groups (7). Turkey has one of the longest waiting periods (12 hours) between the two clinical examinations used to make the diagnosis (8).

This two-centered retrospective study performed in Van, one of the biggest cities in eastern Turkey, aimed to evaluate the process from diagnosis to organ transplantation, the diagnosis duration of BD, tests used in diagnosis, donor ratios, and the factors affecting organ quality.

## Materials and Methods

This study was conducted after obtaining local ethical approval (approval number: 2017/6) in the Van Yuzuncu Yil University Hospital's ICU and in a Private Istanbul Hospital's general ICU. Patients' files

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and computer records of patients whose BD diagnosis was made by the same organ transplantation coordinator were evaluated retrospectively. The cases with BD diagnosis between January 2012 and April 2017 were included in the study. When the centers' characteristics were evaluated during the study period, University Hospital had 662 beds. The number of third-degree ICU beds was 79, and the number of beds in the anesthesia ICU was 14. The Private Hospital was a 185-bed hospital, with a total of 14 beds in the third-level general ICU. Between 2012 and 2014, BD diagnosis was made by a four-membered physicians committee consisting of an anesthesiologist, a neurologist, a neurosurgeon, and a cardiologist, according to the regulations of law number 2238 on organ harvesting, storage, and transplantation (9). After 2014, BD diagnosis was made by a two-membered committee consisting of a neurologist or neurosurgeon and an anesthesiologist or intensivist, according to law number 28886 (10).

A total of 78 cases with BD were identified. Twenty-one patients with incomplete data and lack of consent of the coordinator who made the diagnosis were excluded from the study. Fifty-one patients who had BD diagnosis by an organ and tissue transplantation coordinator were included in the study. The genders, ages, reasons of hospitalization, causes of death, apnea test performance, imaging methods used, length of stay in the ICU, time for diagnosis of BD, donor status, and routine laboratory data of the cases were evaluated.

**Statistical Analysis:** SPSS Windows 23.0 statistical package program was used to analyze the data. Demographic data were analyzed descriptively. Descriptive statistics for continuous variables were expressed as mean, standard deviation, and minimum and maximum values, while categorical variables were expressed as numbers and percentages. A  $p$  value of  $<0.05$  was considered statistically significant.

## Results

Fifty-seven patients with BD were included in the study. The demographic data, hospitalization diagnoses, supportive tests used in diagnosis, and length of hospital stay of the cases are shown in Table 1. The number of beds in the hospitals, the number of BD diagnoses per year, and the status of the donors are shown in Table 1. The patients' hospitalization diagnosis according to age group is presented in Figure 1.

When the patients' BD time was evaluated, the average diagnosis length was 70.5 hours (min 24, max 240) in 84.2% ( $n = 48$ ) of the patients. In 10.5% of the cases ( $n = 6$ ), diagnoses were made in 188 hours

(min 168, max 216), and in 5.3% ( $n = 3$ ) of the cases, the diagnosis was made in 616 hours (min 360, max 1032). When the cases that accepted organ transplantation ( $n = 5$ ) were evaluated, the average BD diagnosis time was 60 hours (min 24, max 120) in 80% ( $n = 4$ ) of the patients and 360 hours in 20% ( $n = 1$ ). The mean time to cardiac arrest after BD diagnosis was found to be 37.8 hours (min 4, max 96). All laboratory tests remained within normal limits during the hospitalization period, but the International Normalized Ratio (INR) values increased as the days of admission increased.

## Discussion

According to the world standards, at least one BD report in a year should exist per ICU bed with a ventilator (11). The total number of university hospital, state hospital, and private hospital beds is 33,063 in Turkey. Although approximately 4600 of these beds are intensive care beds with a ventilator, 2178 BDs were reported in Turkey, and only 27.5% ( $n = 598$ ) of these were used as donors, according to the national data of 2018 (4). Also in this study, BD diagnosis was found to be lower, similar to the data to the Turkey's 2019 statistical data, than the international values.

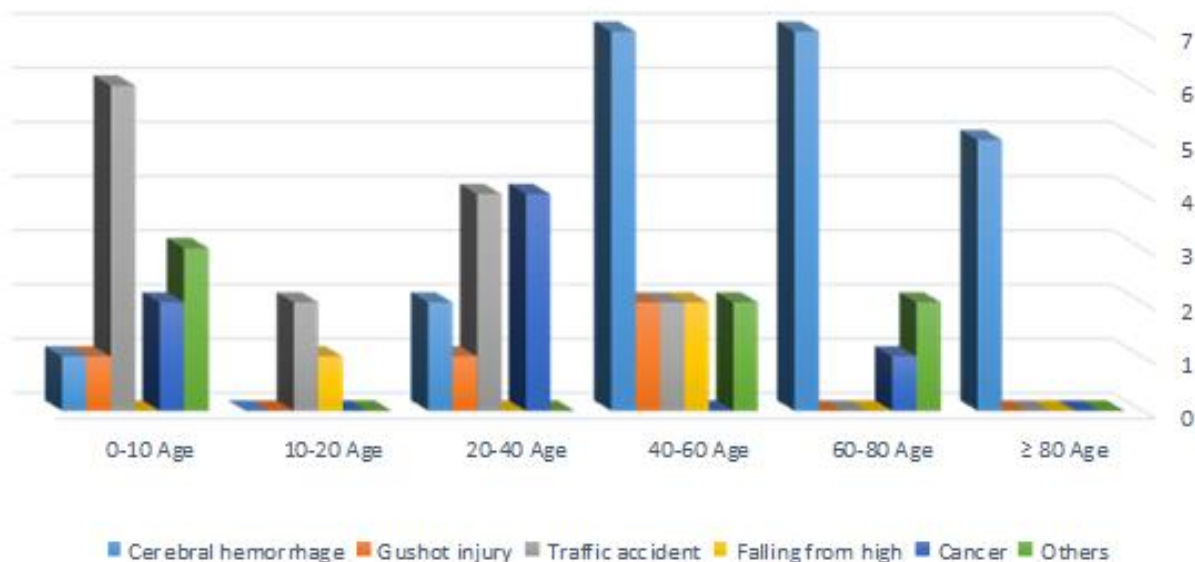
Studies have indicated that a short duration for BD diagnosis would lead to an increase in organ donation acceptance rates (6). Halitoglu et al. found the mean time from hospitalization to the diagnosis of BD was 57 hours. In cases who did not accept organ donation, they reported that the median time of diagnosis was 86.8 hours. However, this difference was not statistically significant (12). Kirakli et al. evaluated the effect of BD diagnosis length on organ donation and found that the mean duration of BD was 6 (5 to 16) hours in cases that were given family permission and 22 (6 to 90) hours in cases without permission for organ donation ( $p = 0.03$ ) (5). In this study, the duration of diagnosis was found to be shorter in patients who accepted organ donation than those who did not. However, the duration of BD diagnosis was found to be longer than in the current literature.

The Regulation on Organ Transplantation and Tissue Transplantation of 2012 (no. 28191), which is currently in use, requires the implementation of a supporting test for the diagnosis of BD. A test to evaluate brain blood flow should be performed in cases in which an apnea test cannot be performed (13). In this study, tests evaluating brain blood flow were used in all cases. The most commonly used imaging technique, due to its rapidity, was CT angiography (CTA), with a rate of 75.4% ( $n = 43$ ).

**Table 1.** The demographic data, hospitalization diagnoses, supporting tests, length of stay in hospital of BD cases

Parameters	Results
Age, (year)	40,75±26.5
Male, n (%)	36 (63.2)
Female, n (%)	21 (36.8)
Hospitalization diagnosis, n (%)	
Cerebral hemorrhage	22 (38.6)
Trauma	16 (28.1)
Cancer	7 (12.3)
Gunshot injury	4 (7)
Falling from high	3 (5.3)
Others	5 (8.8)
Supportive Test, n (%)	
CTA	43 (%75.4)
MRA	10 (17.6)
TD	4 (%7)
Apnea test usage, n (%)	
Yes	42 (73.7)
No	15 (2.,3)
Donor status, n (%)	
Yes	5 (8.78)
No	52 (91.2)

**CTA:** Computerized tomography angiography, **MRA:** Magnetic resonance angiography **TD:** Transcranial doppler ultrasonography



**Fig. 1.** Hospitalization diagnosis according to age

Although CTA is cheaper and more accessible than Magnetic Resonance Angiography (MRA), there is no difference in terms of diagnostic values as a supporting test used to confirm the diagnosis. The main challenges of these tests are transportation of

the patient out of the ICU and requirement of contrast material and intervention (14). In a review study in 2014, Taylor et al. stated that CTA correctly identified 85 out of 100 cases with positive clinical test results (15). Based on these results, CTA is not

accurate enough to be a mandatory test. Recommended supportive diagnostic tests are used at higher rates, but these should only be used in cases of difficulty in diagnosing BD.

Transcranial Doppler (TD) stands out as a noninvasive and reproducible test that can be performed bedside. The disadvantages of this method include the risk of failure of the temporal window imagination in adult patients (8%), the inability to apply the test to patients who had decompressive surgery, and the experience required to perform the test (14, 16). In this study, 7% (n = 4) of the patients who were clinically diagnosed with BD were supported with TD.

In a retrospective study performed by Halitoglu et al. in Sanliurfa, a Southeastern Anatolian city, 92 cases with a diagnosis of BD were evaluated in 2018. They reported that 12% (n = 8) of the cases could be used as a cadaveric donor and that the rate of donation from Sanliurfa was 1.86 PMP (12). Oksuz et al. reported that 34.48% (n = 10) of the BD cases were donors and that the mean duration of evaluation with TD was  $6.74 \pm 19.76$  hours (min 1, max 48) (7). In a study conducted in Izmir in 2011, Kirakli et al. found that 69% (n = 33) of the relatives of patients gave permission to donate the organ. In this study, this rate was low (8.8%).

Significant differences exist between the regions of Turkey; the organ donations in Aegean and Mediterranean regions are higher than other regions in Turkey. In Southeastern and Eastern Anatolia, the donation ratios from cadavers for PMP are relatively low according to the general situation in Turkey. Van is a city with a donation ratio for PMP of 1.10 (4). The reasons for a low number of donors in this study may be due to religious beliefs or hope of improvement for the donor candidate patients in the patient's relatives, due to poor understanding of BD as an irreversible process or poor explanation of the condition (17).

For organ donation in Turkey, open approval (i.e., the agreement model) is applied. According to law number 2238, the organ donor's consent for donation must be received before death, or the relatives must consent if the patient did not declare his/her intention for donation (8). However, in regulation 24066, the donation cannot be performed without the consent of his/her relatives, even if the person has an organ donation card (18). This may be another reason for the low number of donors.

The supportive therapy termination authority to the patient with BD diagnosis was belonged to the physicians performing treatment to the patient after BD diagnosis to the patients' relatives in previous

regulations in Turkey. But the later regulation left this authority to the physician after the relatives' acceptance to supportive therapy termination (13). This change in regulation leads the physicians to uncertainty in terminating the treatment of patients with BD diagnosis. Oksuz et al. found the life expectancy of patients after the diagnosis of BD was 4 (2 to 70) hours (8). In this study, the duration of ICU stay was not prolonged after diagnosis.

In conclusion, diagnosis time was found to be longer than the literature presented, and CTA was the most commonly used imaging modality in addition to the apnea test. Additionally, rates of donation were low in the city. To increase the number of organ transplants from cadavers in this country, the diagnosis of BD should be made faster. Therefore, the use of tests to ensure the effective and rapid execution of the diagnostic process should be expanded.

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