



Öznur Uludağ,
Ülkü Sabuncu,
Hatice Kuşderci,
Fikriye Kaplan,
Atilla Tutak,
Mevlüt Doğan

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Öznur Uludağ, Atilla Tutak, Mevlüt Doğan
Adıyaman University Faculty of Medicine,
Department of Anesthesiology and Reanimation,
Adıyaman, Turkey

Ülkü Sabuncu
Ankara High Specialized Training and Research
Hospital, Clinic of Anesthesiology and Reanimation,
Ankara, Turkey

Hatice Kuşderci
Bandırma State Hospital, Clinic of Anesthesiology and
Reanimation, Balıkesir, Turkey

Fikriye Kaplan
Adıyaman University Training and Research Hospital,
Organ and Tissue Transplant Coordinator,
Adıyaman, Turkey

Öznur Uludağ (✉),
Adıyaman University Faculty of Medicine,
Department of Anesthesiology and Reanimation,
Adıyaman, Turkey

E-mail : uludagoznur@gmail.com
Phone : +90 416 223 16 90 - 1340

Where are We on Organ Donation?

Organ Bağışında Neredeyiz?

SUMMARY *Objective:* It was aimed to present the acceptance rate of organ donation of cases that were diagnosed with brain death and evaluated in terms of their demographic and clinical properties retrospectively in Adıyaman University Training and Research Hospital.

Material and Method: In the intensive care unit of our hospital, cases that were diagnosed with brain death between the dates of January 2008 and December 2014 were retrospectively analyzed. Cases were evaluated in terms of age, sex, cause of brain death, blood groups, donation status, reasons for acceptance or rejection of donation, cardiac arrest, vasopressin treatment, laboratory test results, arterial blood gas values before and after the apnea test, intensive care unit follow-up durations, apnea test, seasonal and annual distribution. Also, potential donors and recipients were analyzed in accordance with their demographic characteristics.

Results: The diagnosis of brain death was made in totally 57 cases; of those, 34 (59.6%) were men and 23 (40.4%) were women. The most common causes for brain death were traumatic subarachnoid hemorrhage (SAH) and intracerebral hematoma. Most of the cases had A Rh+ blood type (n=18, 31.5%) and the rate of brain death was 4.7 times higher in Rh (+) patients in comparison to Rh (-) patients. The rate of incidence of cardiac arrest was 12.3% (n=7), and it was more common in traumatic SAH patients. The rate of receiving vasopressor therapy was 21.1% (n=12), and the mean duration of therapy was 1.3±0.8 days. It was more commonly used in traumatic SAH patients (n=10). The follow-up period was 2.7±3.2 (minimum: 1, maximum: 17) days. Five patients were considered to be organ donors. The most common reason for acceptance of donation was the effect of organ transplantation coordinator during family interviews (n=3, 60%). In total, 4 livers, 5 kidneys and 1 heart transplantation operations were performed to 10 patients.

Conclusion: Due to problems in organ donation, patients that might be potential organ donors must be transferred to intensive care unit and taken under critical patient care since then, and brain death should be considered in patients with Glasgow coma scale <7. The raising the awareness and training of the staff in intensive care units about the recognition of brain death and donor care are also important. Also, the interview with the families must be performed by an experienced coordinator to increase the rate of acceptance of donation and raise the awareness of the community regarding the organ donation.

Keywords: Brain death, intensive care unit, apnea test, tissue and organ transplantation

ÖZ *Amaç:* Adıyaman Üniversitesi Eğitim ve Araştırma Hastanesi, yoğun bakım ünitesinde beyin ölümü tanısı konulan olguların demografik ve klinik özellikleri retrospektif olarak incelenerek, organ bağışı kabul oranları sunuldu.

Gereç ve Yöntem: Hastanemiz yoğun bakım ünitesinde 2008-2014 yılları arasında beyin ölümü tanısı konmuş hastalar retrospektif olarak incelendi. Tüm hastalar; yaş, cinsiyet, beyin ölümü nedeni, kan grubu, organ bağışı kabul ve red nedenleri, kardiyak arrest geçirme ve vazopressin kullanma durumu, laboratuvar testleri, apne testi öncesi ve sonrası kan gazı değerleri, yoğun bakımda izlem süresi, apne testi, yıl ve mevsimsel dağılım açısından değerlendirildi. Donör adayları olan olgular verilen organ ve alıcı olan hastalar demografik özelliklerine göre ayrıca değerlendirildi.

Bulgular: Otuz dört (%59,6) erkek, 23 (%40,4) kadın toplam 57 hastaya beyin ölümü tanısı konuldu. En sık nedenler travmatik subaraknoid kanama (SAK) ve intraserebral hematoma idi. Olguların çoğu A Rh (+) kan grubunda (n=18, %31,5) idi. Rh (+) hastalarda Rh (-) hastalara oranla 4,7 kat fazla beyin ölümü tespit edildi. Kardiyak arrest görülme oranı %12,3 (n=7) olup en sık

travmatik SAK (n=5) hastalarında görüldü. Vazopressör tedavi kullanma oranı %21,1 (n=12), vazopressör kullanım günü $1,3\pm 0,8$ olarak bulundu. En sık travmatik SAK hastalarında (n=10) kullanıldı. Yoğun bakımda izlem süresi $2,7\pm 3,2$ (minimum: 1, maksimum: 17) gündür. Beş hasta organ donörü olarak kabul edildi. En sık kabul nedeni aile görüşmesinde koordinatör etkisi (%60, n=3) idi. Toplam 10 hastaya dört karaciğer, beş böbrek, bir kalp nakli gerçekleştirildi.

Sonuç: Organ transplantasyonunda yaşanan sıkıntılardan dolayı potansiyel donör olabilecek hastalar yoğun bakıma yatırıldıkları andan itibaren kritik hasta bakımına alınmalı ve Glasgow koma skalası 7'nin altında olan her hastada beyin ölümü gelişebileceği düşünülmelidir. Yoğun bakım çalışanlarının beyin ölümünü tanıma ve donör bakımı konusunda bilinçlendirilmesi ve eğitilmesi, aile görüşmelerinin deneyimli bir organ nakli koordinatörü tarafından yapılması ve toplumun bilinçlendirilmesi ülkemizde organ bağıışı oranlarını artırabilir.

Anahtar Kelimeler: Beyin ölümü, yoğun bakım ünitesi, apne testi, doku ve organ nakli

Introduction

Brain death is a clinical diagnosis and it is defined as total and irreversible loss of all brain and brainstem functions. Prerequisites for brain death diagnosis are determination of the cause of coma, determination of irreversible and total nature of brain damage, presence of core body temperature ≥ 32 °C, absence of hypotensive shock, exclusion of drug effects and intoxications which may cause reversible coma, and absence of metabolic, electrolyte or acid-base disturbances. When these conditions are met, state of a deep coma, inability to evoke brain stem reflexes, and absence of spontaneous breathing effort are looked for. Pupils are generally irresponsive to bright light, at midline and dilated (4-9 mm). Oculocephalic and vestibulocochlear reflexes are absent. Cornea reflex and pharyngeal, and tracheal reflexes are also absent (1).

Brain death was first defined by Mollaret and Goulon (2) and was named as 'coma depasse'. It was legally accepted in United States in 1970 by state of Kansas. In United Kingdom British Criteria were published in 1976 and were accepted as a bill in 1979 (3).

In Turkey brain death diagnosis is made according to law 2.238 About Organ and Tissue Donation, Preservation, Vaccination, and Transfer. Based on this law Legislation of Organ and Tissue Transplantation Services came into effect after being published in Official Journal number 28886 at 01.02.2012. Eleventh article of this legislation was changed in 18.01.2014. According to this legislation, two doctors, one of them being a neurologist or neurosurgeon and the other being an anesthesiologist or an intensive care specialist, can decide brain death with a consensus.

Apnea test should be performed to every patient by an anesthesiologist or an intensive care specialist in order to diagnose brain death. To perform an apnea test, preconditions such as normothermia, normotension, and normovolemia should be achieved. Under these conditions PaCO₂ should be kept at 35-45 mmHg and PaO₂ above 200 mmHg. After these conditions are achieved the patient is

weaned from mechanical ventilator and intra tracheal oxygen is applied. After the test, if spontaneous breathing is absent despite a PaCO₂ value ≥ 60 mmHg and/or increase in PaCO₂ ≥ 20 mmHg, apnea test is considered to be positive (1).

The aim of this study is to determine the demographic and clinical characteristic of the brain death cases and to provide acceptable rates of organ donation in Adiyaman University Research and Education Hospital.

Material and Method

After approval is obtained from Ethics Committee of Adiyaman University Faculty of Medicine (57831858/2), cases who were diagnosed as brain death between 2008 and 2014 were retrospectively evaluated. All cases were assessed for age, sex, reason of brain death, blood group, reasons for acceptance or rejection of donation, status of cardiac arrest and vasopressin use, laboratory tests, ejection fraction (EF), blood gas analyses before and after apnea test, duration of intensive care unit stay, seasonal and annually variation, apnea test, and vasopressin test. Donors and recipients of donations were also evaluated according to donated organ and sociodemographic features.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) 21.0 was used for statistical evaluation of data obtained from the study. Mean, standard deviation, and percentage values were calculated as descriptive statistics.

Results

Thirty four (59.6%) of 57 patients detected to have brain death between 2008 and 2014 were males and 23 (40.4%) were females. Mean [\pm standard deviation (SD)] age of the patients was 48 ± 23 (range 2-87) years and median was 52 years. Mean age of male patients was 44.2 ± 24.3 and female patients was 54.0 ± 21.2 . Brain death was more common in males although females were older. The average time of the

patients was 3.70 ± 2.12 days after admission to the intensive care unit until the determination of the Glasgow coma scale was 3. Time period between the determination of gamma knife radiosurgery was 3 and the diagnosis of brain death 2.75 ± 1.97 days. Brain death patients were followed in intensive care unit by anesthesiology and reanimation department.

The most common reasons for brain death were traumatic subarachnoid hemorrhage (SAH) (n=24, 42.1%) and intracerebral hematoma (n=8, 14%) (Table 1).

Most of the brain death patients had A Rh (+) blood group (n=18.31, 5%). O Rh (+) and A Rh (+) blood groups were most commonly observed in males and B Rh (+) blood group was most commonly observed in females. When brain deaths were analyzed according to Rh groups Rh (+) patients had 4.7 times more brain deaths than Rh (-) patients. A Rh (-) patients were the oldest and B Rh (-) patients were the youngest (Table 2).

Brain death diagnosis was made in 57 cases and organs were donated in 5 (8.7%) patients. Two of the organ donors

were males and 3 were females. Mean (\pm SD) age of the donors was 51 ± 19 . Two patients were O Rh (+), 2 patients were A Rh (+), and 1 patient was AB Rh (+). When we evaluate reasons for acceptance of organ donation, effect of organ transplantation coordinator during family interview was the most important factor in 60% (n=3) and thought of helping to people in need of transplantation was the most important factor in 40% (n=2) of cases. Reasons for rejection of organ transplantation were rejection by the family 51.9% (n=27), discordance in the family 36.6% (n=19), ambivalence in the family 5.8% (n=3), spiritual reasons 1.9% (n=1), inability to reach patient's relatives 1.9% (n=1) and patient's will against donation 1.9% (n=1). Transplantations of 4 livers, 3 right kidneys, 2 left kidneys, and a heart were performed to 5 males and 5 females in İnönü, Hacettepe and Başkent University Hospitals (Table 3).

Cardiac arrest was not observed in 87.7% (n=50), and observed in 12.3% (n=7) of the patients. Cardiac arrest was seen in patients who had traumatic SAH (n=5),

Table 1. Causes of brain death, age and sex of the cases

Diagnosis	Number (n)	Percentage (%)	Male (n)	Female (n)	Mean age
Traumatic SAH	24	42.1	16	8	46.5
Intracerebral hematoma	8	14.0	6	2	58.3
Hypoxic encephalopathy	6	10.6	2	4	57.6
Intraventricular hemorrhage	5	8.7	3	2	40.6
Subdural hematoma	5	8.7	3	2	35.0
Cerebral infarction	2	3.5	2	0	69
Hypertensive SAH	2	3.5	0	2	71.5
Head trauma	2	3.5	1	1	53.0
Hydrocephalus	1	1.8	0	1	33
Cranial firearm injury	1	1.8	0	1	21.0
Frontoorbital fracture (motorcycle accident)	1	1.8	1	0	18

SAH: Subarachnoid hemorrhage

Table 2. Sex and mean age distributions of the cases according to blood groups

Blood group	Case number	Percentage	Male	Female	Mean age
O Rh (+)	15	26.3	11	4	41.7 \pm 22.2
O Rh (-)	3	5.3	2	1	38.0 \pm 19.9
A Rh (+)	18	31.5	11	7	54.6 \pm 19.3
A Rh (-)	4	7.0	3	1	60.0 \pm 25.6
B Rh (+)	11	19.3	3	8	53.2 \pm 27.5
B Rh (-)	2	3.5	2	0	18.0 \pm 0.0
AB Rh (+)	3	5.3	1	2	52.3 \pm 26.0
AB Rh (-)	1	1.8	1	0	45.0 \pm 0.0
Total	57	100	34	23	48.4 \pm 23.3

hydrocephalus (n=1), intracerebral hematoma (n=1), and hypoxic encephalopathy (n=1). Mean age of patients who had cardiac arrest was 44.5±18.7 years, and who didn't have cardiac arrest was 49.0±24.1 years. Cardiac arrest was observed to occur in younger patients. Cardiac arrest was seen in 4 males and 3 females. Blood groups of patients who had cardiac arrest were 0 Rh (+) (n=2), 0 Rh (-) (n=2), A Rh (+) (n=2), and B Rh (+) (n=1).

Rate of vasopressor treatment was 21.1% (n=12). Vazopressor treatment was not used in 78.9% (n=45) of patients. Duration of vasopressor treatment use was 1.3±0.8 days. Vazopressor treatment was used to patients who had traumatic SAH (n=8), head trauma (n=1), hydrocephalus (n=1), hypoxic encephalopathy (n=1), and multiple trauma due to traffic accident (n=1). Mean age of patients who had vasopressor treatment was 44.5±23.6 and who didn't have vasopressor treatment was 49.6±23.4. Vazopressor treatment was applied to younger patients.

Mean systolic arterial pressure in patients was 120.1±31.2 and mean diastolic arterial pressure was 72.5±18.5 and mean pulse rate was 84.5±18.3 (Table 4, 5).

Apneic oxygenization method is used to demonstrate that respiratory drive is absent. Apnea test was performed in all patients; nevertheless, it was observed that apnea test could not be completed in four patients. Supporting test wasn't used. Mean age of the patients that had an apnea test was 22.6±3.2 and who didn't have an apnea test was 35.0±17.5. Diagnoses of the patients who didn't have apnea test were head trauma (n=1), intraventricular hemorrhage (n=1), intracerebral hematoma (n=1) and multiple trauma after a traffic accident (n=1) (Table 6).

Mean (±SD) EF was 52.7±8.4 (minimum: 32, maximum: 70).

Mean (±SD) duration of follow up was 2.7±3.2 (minimum: 1, maximum: 17) days. Mean (±SD) intensive care unit stay

of male patients was 2.5±2.5 days, and female patients was 3.0±4.0 days. Brain death diagnoses were most commonly made in years 2013 and 2014 (Table 7).

Number of brain deaths was highest in fall and lowest in winter (Table 8).

Discussion

The most common causes of cardiopulmonary arrest in adults are anoxic brain injury which develops during cardiopulmonary arrest, traumatic brain injury, subarachnoid and intracerebral hemorrhages, and ischemic injury. Although much rarer in adults, fulminant encephalitis and bacterial meningitis are among other reasons of brain death (4). In children the reasons are motor vehicle accidents, asphyxia, and especially in Western countries trauma due to child abuse (5). In our study most common causes were traumatic SAH (42.1%), intracerebral hematoma (14.0%), and hypoxic encephalopathy (10.6%). Seven of our patients had brain injury due to traffic accidents, and 1 had brain injury due to electric shock. Whatever the cause is, the pathophysiologic process is the same. Brain trauma or cerebrovascular injury causes brain edema and increased intracranial pressure. When increased

Table 3. Ratios for organ transplantation

Organ donation	Male (n)	Female (n)	Mean age (mean ± SD)
Reject	32	20	48±13
Accept	2	3	51±19

SD: Standard deviation, Data presented as mean ± SD

Table 4. Hemodynamic parameters in cases

	Mean ± SD	Minimum	Maximum
SAP	120.1±31.2	50	220
DAP	75.5±18.5	20	110
Pulse	84.5±18.3	40	120

SAP: Systolic arterial pressure, DAP: Diastolic arterial pressure, SD: Standard deviation

Table 5. Mean (±SD) of parameters of brain death cases after diagnosis of brain death

Parameter	Mean ± SD	Parameter	Mean ± SD
Glucose	160.2±58.6	Sodium	147±15.2
Urea	68.3±52.0	Potassium	4.0±0.9
Creatinine	1.8±1.4	Chloride	113.8±13.3
Total protein	6.0±0.9	Calcium	8.6±0.8
Albumin	3.0±0.7	Leukocyte	13.2±5.5
AST	79.2±126.4	Hemoglobin	11.7±2.2
ALT	78.2±150.2	Hematocrit	35.3±7.8
ALP	76.8±50.2	Platelet	187±81.4
CK	571.1±1081	PT	17.1±8.4
CK-MB	88.3±141.6	INR	2.0±1.9

AST: Aspartate aminotransferase, ALT: Alanin aminotransferase, ALP: Alkaline phosphatase, CK: Creatine kinase, CK-MB: Creatine kinase-MB, SD: Standard deviation, PT: Prothrombin time, INR: International normalized ratio, All data presented as mean ± standard deviation

Table 6. Blood gas values of the cases before and after apnea test

Apnea test	PH	PaO ₂	PaCO ₂	HCO ₃	Saturation
Pre-test	7.2±0.1	261.0±141.1	44.6±26.6	21.0±4.7	98.1±3.8
Post-test	7.1±0.1	143.7±117.7	67.2±23.4	21.6±4.5	90.4±10.9

All data presented as mean ± standard deviation

intracranial pressure exceeds arterial blood pressure cerebral circulation ceases. Then aseptic brain necrosis develops. Increased intracranial pressure causes compression of all brain structures including brainstem and therefore total brain infarct ensues. Increased intracranial pressure and brain stem compression during the process of brain death may cause significant hypertension and bradycardia (Cushing phenomenon). When all brainstem becomes ischemic and irresistible sympathetic stimulation occurs. This leads to tachycardia, hypertension and increased catecholamine levels (autonomic storm) (6). At this stage, tachycardia and hypertension is short-lived and intervention to decrease hypertension is not recommended (7). When intracranial pressure increases arterial blood pressure suddenly decreases. This sudden decrease is a sign of tonsillar herniation via foramen magnum to the spinal cord. Adequate volume replacement is achieved by balanced salt solution, or colloid solution and in some cases blood transfusion. Inotropic agents such as dopamine, epinephrine, and norepinephrine are necessary to maintain blood pressure. Use of vasopressin or catecholamines may help to maintain hemodynamic stability and renal functions of brain death patients (8). In our study rate of vasopressin use was detected to be 21.1% (n=12). Duration of vasopressin use was 1.3±0.8 days. Two studies in our country reported 88% and 74% rates for requirement of vasopressor or inotropic agents due to hypotension (9,10).

Table 7. Number of brain death cases in each year between 2008 and 2014

Year	2008	2009	2010	2011	2012	2013	2014
Case number	3	6	12	3	5	14	14

Table 8. Seasonal distribution of brain death cases

Season	Month	Patient number
Winter n=11 19.3%	December	7
	January	2
	February	2
Spring n=14 24.6%	March	8
	April	6
	May	0
Summer n=13 22.8%	June	4
	July	5
	August	4
Fall n=19 33.3%	September	5
	October	9
	November	5

In our country Brain Death Detection Commissions are consisted of an anesthesiology and reanimation specialist, a neurologist, a neurosurgeon and a cardiologist till 18.01.2014. With today's regulations, brain death is confirmed by consensus of a neurologist or a neurosurgeon and an anesthesiologist or an intensive care specialist. Apnea test is mandatory in our country for brain death diagnosis.

In our study brain death diagnosis was made by apnea test using apneic oxygenation technique. With appropriate mechanical ventilation PaCO₂ of 35-45 mmHg and PaO₂ ≥200 mmHg values were achieved. Then the patient was weaned from the mechanical ventilator. Lack of spontaneous respiration despite PaCO₂ ≥60 mmHg and an increase in PaCO₂ more than 20 mmHg from the baseline value was accepted as a positive test result. Hypoxemia during apnea test may lead to cardiac arrhythmia and hypotension. In these patients, peripheral vasodilatation, and cardiac depression due to carbon dioxide and acidosis are possible causes of hypotension (11). Pre-oxygenation prevents development of complications by improving oxygen transport and eliminating alveolar nitrogen stocks (12). A study retrospectively evaluating 228 brain death cases also used apneic oxygenation technique to perform apnea test (13). In our study blood gas analyses before and after apnea test suggests that apneic oxygenation method is reliable in the presence of appropriate pre-oxygenation. However Paries et al. (14) showed that apnea test damages respiratory functions and suggested that lung-saving strategies, especially recruitment maneuvers should be routinely used after the test. An article about criteria for selection of receiver-donor for heart transplantation reported that 20-25% of organs, which are very hardly obtained indeed, were lost due to insufficient treatment of physiopathological responses occurred after brain death (15).

Brain death cases included patients who had mechanical ventilator support in intensive care units. Detection of brain death is important to adjust treatment of patients and to realize organ transplantation probability. Number of patients awaiting organ transplantation is increasing worldwide and rate of organ donation is increasing gradually. Unfavorable outcomes regarding donation may occur due to loss of potential donors before brain death diagnosis, not giving chance of donation to the family, rejection of donation by the family, and poor management of treatments of potential donors. Due to these problems in organ transplantation patients who may be potential donors should be given critical care starting with their admission to intensive care unit and brain death should be expected in every patient with a Glasgow coma scale <7.

Organ donation process is grouped into 8 steps: detection of potential donor, declaration, controlling medical

contraindications, donor management, getting consent from family, removal of organs, distribution of organs to recipients, survival of organs at in vitro conditions, and transfer to the recipient (16). Most donor losses occur during detection of potential donor, declaration, and familial consent steps. Two studies in US reported that 10% of potential donors are lost because they couldn't be noticed by healthcare workers (17,18). To prevent these intensive care unit workers should be trained and their consciousness should be raised on topics such as detection of brain death and management of potential donors.

In Spain, donor rate is reported to be 33-35/million population (19). Evaluation of Turkish data revealed that 9.016 brain deaths were detected between 2008 and 2014 and 2.236 of them were used as donors with consent of their families (20). In the same time period, 57 brain deaths were detected in Adiyaman and 5 patients were used as donors (Table 9, 10).

Establishment of National Coordination Center within Ministry of Health in 2001 lead to an important increase in numbers of both cadaver donors and transplantations (21). In our study an educated and experienced organ transplantation coordinator was among the most important factors in approval of organ transplantation by families.

Brain death cases whose families give consent for donation are reported to local coordination centers. Under the guidance of organ transplantation coordinator necessary tests such as blood group, hepatitis markers, liver and kidney function tests, and echocardiography for patients who can be heart donors were performed with the guidance of organ transplantation coordinator.

Table 9. Brain death data in Turkey between 2008 and 2014

Years	Familial approval		Familial rejection	Number of brain deaths
	Used	Not used		
2008	242	20	458	720
2009	261	37	658	956
2010	269		781	1050
2011	333		958	1291
2012	345		1133	1478
2013	379		1326	1709
2014	407		1405	1812
Total	2236		6719	9016

Table 10. Brain death data in Adiyaman between 2008 and 2014

Years	Familial approval		Familial rejection	Number of brain deaths
	Used	Not used		
2008	1		2	3
2009	1		5	6
2010	1		11	12
2011			3	3
2012	1		4	5
2013	1		13	14
2014			14	14
Total	5		52	57

Conclusion

There is a working organ transplantation program in Turkey but it depends on donations from live donors. Main target is to increase donor pool from cadavers. To achieve this familial rejection rate should be decreased and brain death detection rate should be increased. Cooperation of intensive care unit specialists and organ transplantation coordinators and education of public about organ donation are also important.

Ethics

Ethics Committee Approval: Approval was obtained from ethics committee of Adiyaman University Medical School (29.01.2015, 57831858/2), Informed Consent: This study retrospective.

Peer-review: Externally and Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Öznur Uludağ, Ülkü Sabuncu, Hatice Kuşderci, Mevlüt Doğukan, Atilla Tutak, Concept: Öznur Uludağ, Ülkü Sabuncu, Design: Öznur Uludağ, Hatice Kuşderci, Data Collection or Processing: Öznur Uludağ, Fikriye Kaplan, Analysis or Interpretation: Öznur Uludağ, Mevlüt Doğukan, Literature Search: Öznur Uludağ, Atilla Tutak, Writing: Öznur Uludağ.

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