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Evaluation of organ donation process and affecting factors in COVID-19 pandemic

Gökhan Kılınç[1,2], Fuat Çöken[2]

[1]*Department of Anesthesiology and Reanimation, Atatürk City Hospital, Balıkesir, Turkey;* [2]*Department of Organ and Tissue Transplantation, Atatürk City Hospital, Balıkesir, Turkey ;*

ABSTRACT

Objectives: More than six million people worldwide are affected by end-stage organ failure and the COVID-19 pandemic has dramatically changed organ and tissue donation.

Methods: The data of patients diagnosed with brain death between July 2018-March 2020 (pre-pandemic period) and April 2020-December 2021 (pandemic period) were analyzed retrospectively. Donor characteristics, laboratory levels, time from intensive care admission to determination of brain death, time to family approval, family approval rates and organ types were analyzed.

Results: The mean age of 56 patients with pre-pandemic diagnosis of brain death was 61.82 ± 21.39 years, 37 (63%) patients were donors and 53 organs were obtained. Mean age of 39 patients diagnosed with brain death during the pandemic was 58.26 ± 18.02 years and 38 organs were obtained from 21 (52.5%) donors. Between the two periods, there was a decrease of 30.35% in the diagnosis of brain death, 43.24% in the number of donors and 26.41% in the number of organs supplied. The most common cause of brain death was intracranial hemorrhage during both periods. While the time elapsed between family interview and surgery was 9.33 ± 2.19 hours before the pandemic, it was 15.29 ± 4.28 hours during the pandemic period ($p = 0.01$). There was a significant difference between C-reactive protein levels at the time of diagnosis of brain death ($p < 0.05$). *Staphylococcus haemolyticus* was most frequently seen in blood culture.

Conclusions: Brain death and organ donation have decreased significantly during the pandemic period compared to previous years, similar to research conducted in different countries and regions. Due to COVID-19, prolonged stays in the intensive care unit (ICU) may pose a risk of infection in ICU donors, and care should be taken in terms of donor loss.

Keywords: Organ transplantation, organ donation, transplant surgery, infectious diseases, COVID-19, family consent, brain death

More than six million people worldwide are affected by end-stage organ failure. With the development of the transplantation field, the survival and quality of life of patients with end-stage organ failure has changed. It has changed the lives of these patients as a life-saving treatment method in end-stage organ failure. With all these developments, cadaver donor pools are still insufficient. Accurate and timely detection of brain death is of critical importance in terms of dissemination of organ donations and ensuring the

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Address for correspondence: *Gökhan Kılınç, MD., Atatürk City Hospital, Department of Anesthesiology and Reanimation, Gaziosmanpaşa Mah., 209. Sok., No:26, 10100 Altıeylül, Balıkesir Turkey. E-mail: gkilinc35@hotmail.com, Phone: +90 266 460 40 00, Fax: +90 266 460 40 45*

continuity of transplantation processes, especially heart and lung, which can be done through cadaver donors [1]. Organ procurement from living donors presents some difficulties. With the increasing importance of organ donation from cadavers, the importance of brain death diagnosis, organ donation and donor care has increased even more. It is characterized by the clinical condition that includes irreversible brain death with loss of cerebral function, apnea and absence of brainstem reflexes [2]. In many countries, the guidelines of the American Academy of Neurology are used as an example for brain death conditions, diagnosis and supportive tests [3].

There have been significant medical and technological advances in intensive care. Despite all these developments, the inability to diagnose brain death causes insufficient organ donation. This poses a serious problem for patients awaiting organ transplants. Early detection of potential donors, successful organ donation from families, and correct management of these donors are issues that need to be emphasized. Poor care of potential donors, prolonged family approval and donation process may lead to organ loss [4, 5].

Announced on March 11, 2020, the COVID-19 pandemic has dramatically changed organ and tissue donation. COVID-19 presents some difficulties in harvesting organs from living donors. With the increasing importance of cadaveric organ donation, the importance of brain death diagnosis, organ donation and donor care has increased even more. Recipients are at increased risk due to immunosuppressive drugs, prolonged hospital stay, and possible transmission from asymptomatic infected donors. In addition, there is a risk of contamination for health personnel working in organ transplantation. The risk of transmitting COVID-19 by organ transplant of an organ donor, who is infected with SARS-CoV-2, is still unknown. Transmission is affected by the incubation period of the virus, the degree of viremia, epidemiological risk factors, and viability in blood and organs. Also, real-time PCR, which is commonly used for laboratory confirmation of COVID-19, is not 100% sensitive. In this context, it is recommended to follow the guidelines published by the National Organ and Tissue Transplantation Organization [6]. We evaluated the COVID-19 pandemic process and tried to draw attention to the differences with the pre-pandemic period so that it can be corrected.

METHODS

Patient Characteristics

The medical records of patients diagnosed with brain death in the Intensive Care Unit of Balıkesir Atatürk City Hospital between July 2018 - March 2020 (pre-pandemic period) and April 2020 - December 2021 (pandemic period) were retrospectively reviewed and donor characteristics (gender, age, cause of brain death), Glasgow Coma Scale scores at intensive care unit admission, time from intensive care unit admission to determination of brain death and time from family consent to procurement, family consent rates and organ types were analysed by anonymising details. The results of C-reactive protein (CRP), white blood cell count (WBC), blood sodium (Na), Creatinine levels and cultures (tracheal aspirate, urine and blood) were evaluated on the day of admission to the intensive care unit and the day of diagnosis of brain death.

COVID-19 Period Brain Death Diagnosis and Evaluation

During the pandemic process, potential donors were screened for COVID-19 according to the recommendations of the Scientific Committee of the Ministry of Health. Real-time polymerase chain reaction (RT-PCR) tests were required according to this instruction. SARS-CoV-2 RT-PCR tests were requested at least twice at 24-hour intervals from the patients' intratracheal aspirate samples. The patient's data was reported to the National Coordination Center by the transplant coordinators together with the SARS-CoV-2 RT-PCR results. All donors had at least one thorax computed tomography scan performed during hospitalization. All organ donors were consulted by Infectious Diseases and Clinical Microbiology doctors and Chest Diseases doctors for suspected COVID-19.

Ethical approval was obtained for the study from the local ethics committee of Balıkesir University (Date: 07.09.2022, Decision no: 2022/100). This study was conducted in accordance with the tenets of the Declaration of Helsinki Principles.

Statistical Analysis

Statistical analysis was performed using Statistical Package for the Social Sciences 20.0 software (Statistical Package for the Social Sciences version 20, IBM Corp., Armonk, New York, IL, USA) software. Whether the variables fit the normal distribution or not was evaluated with the Kolmogorov - Smirnov test. Student -t test was used for the comparisons between groups of normally distributed continuous data. Parametric data with normal distribution were presented as mean ± standard deviation (SD). Values with $p < 0.05$ were considered statistically significant. Categorical variables are presented as frequency and percentages.

RESULTS

The mean age of 56 patients diagnosed with brain death before the pandemic was 61.82 ± 21.39 years, 37 (63%) patients were donors and 53 organs were recovered. Mean age of 39 patients diagnosed with brain death during the pandemic was 58.26 ± 18.02 years and 38 organs were obtained from 21 (52.5%) donors. The procured organ details are shown in Table 1. Between the two periods, there was a decrease of 30.35% in the diagnosis of brain death, 43.24% in the number of donors and 26.41% in the number of organs procured. 51.6% of the patients were male and 48.4% were female. In the pre-pandemic period, one patient died while distribution was ongoing, and organ harvesting was not performed from 13 patients for medical reasons. During the pandemic period, three patients died while distribution was ongoing, and three families did not come to the meeting. Due to the suspicion of COVID-19 in two patients and COVID-19 positive in three patients during the donor preparation process, organ removal procedures were terminated. Organ removal was not performed in three patients for medical reasons, and in one patient due to organ ischemia during surgery. In this process, 2663 of 10999 patients hospitalized in intensive care units were diagnosed with COVID-19.

The most common cause of brain death was intracranial haemorrhage both before and during the pandemic. While trauma patients were the 2nd in the pre-pandemic period, other intracranial events were in the second rank during the pandemic period (Table 2). While %33.9 of the patients with brain death had A Rh (+) blood group during the pandemic and %28.2 before the pandemic, %28.6 and %28.2 had O Rh (+) blood group and there was no significant difference between blood groups in terms of blood groups (Table 2).

CRP, WBC, Na and Creatinine levels of the patients were scanned and compared with each other at the time of hospitalization and at the time of brain death, both before and during the pandemic. A statistically significant difference was found between CRP levels at the time of diagnosis of brain death before and after the pandemic ($p < 0.05$). When the CRP, WBC, Na and creatinine levels of the patients before and during the pandemic were compared with the levels at the time of intensive care admission and brain death diagnosis, CRP, Na and creatinine levels were higher at the time of diagnosis of brain death, and there was a statistically significant difference. There was no significant difference between WBC levels (Table 3).

The time elapsed between admission to the intensive care unit and diagnosis of brain death was 115.37 ± 89.1 hours and 124.66 ± 152.68 hours before and during the pandemic, respectively. While the time from family interview to surgery was 9.33 ± 2.19 hours before the pandemic, it was found to be 15.29 ± 4.28 hours during the pandemic period, and there is a statistically significant difference ($p = 0.01$) (Table 2).

Blood, urine and tracheal aspirate cultures were sent from potential donors with brain death. In the pre-

Table 1. Organs procured from brain-dead patients

	Before COVID-19 (n = 56)	During COVID-19 (n = 39)
Kidney, n (%)	31 (55.35)	25 (64.10)
Liver, n (%)	19 (33.92)	10 (25.64)
Heart, n (%)	3 (5.35	2 (5.12)

Table 2. Baseline characteristics of patients

	Before Pandemic (n = 56)	During Pandemic (n = 39)	*p* value
Age (years) (mean ± SD)	**61.82 ± 21.39**	**58.26 ± 18.02**	**0.460**
Gender, n (%)			
Male	**30 (53.6)**	**19 (48.7)**	
Female	**26 (46.4)**	**20 (51.3)**	
Primary hospital admission diagnosis, n (%)			
Intracranial hemorrhage	**17 (30.35)**	**17 (43.58)**	
Head trauma	**11 (19.64)**	**2 (5.12)**	
Postcardiorespiratory arrest	**10 (17.85)**	**2 (5.12)**	
Ischemic stroke	**9 (16.07)**	**4 (10.25)**	
Subarachnoid hemorrhage	**5 (8.92)**	**4 (10.25)**	
Blood group, n (%)			
A Rh (+)	**19 (33.9)**	**11 (28.2)**	
0 Rh (+)	**16 (28.6)**	**11 (28.2)**	
B Rh (+)	**14 (25)**	**5 (12.8)**	
A Rh (-)	**3 (5.4)**	**-**	
AB Rh (+)	**3 (5.4)**	**6 (15.4)**	
O Rh (-)	**1 (1.8)**	**3 (7.7)**	
AB Rh (-)	**-**	**2 (5.1)**	
Time from Intensive care unit admission to diagnosis of death (mean ± SD)	**115.37 ± 89.1**	**124.66 ± 152.68**	**0.310**
Time from family interview to surgery (mean ± SD)	**9.33 ± 2.19**	**15.29 ± 4.28**	**< 0.001**

Table 3. Laboratory values of patients diagnosed with brain death

	Before Pandemic	*p* value	During Pandemic	*p* value
CRP (mg/dL) (ICU)	**2.25 ± 4.01**	**< 0.05**	**4.44 ± 6.71**	**< 0.05**
CRP (mg/dL) (BD)	**13.81 ± 14.30**		**14.10 ± 8.48**	
WBC ($\times 10^9$/L) (ICU)	**13.83 ± 6.27**	0.293	**16.83 ± 8.89**	0.658
WBC ($\times 10^9$/L) (BD)	**15.07 ± 8.57**		**16.04 ± 7.24**	
Na (mEq/L) (ICU)	**138.73 ± 4.44**	**< 0.05**	**138.95 ± 4.01**	**< 0.05**
Na (mEq/L) (BD)	**153.75 ± 15.78**		**153.90 ± 18.95**	
Creatinin (mg/dL) (ICU)	**1.33 ± 1.43**	**< 0.05**	**1.31 ± 1.28**	**< 0.05**
Creatinin (mg/dL) (BD)	**1.96 ± 1.48**		**2.09 ± 1.46**	

CRP = C-reactive protein, WBC = white blood cell, Na = Sodium, ICU = Intensive care unit, BD = Brain death

pandemic period, the most common microorganisms were *Staphylococcus haemolyticus* in blood culture, *Escherichia coli* in urine culture, and *Acinetobacter baumanii*, *Burkholderia cepacia*, *Staphylococcus aureus* in tracheal aspirate. During the pandemic period, *S. haemolyticus* was the most common in blood culture, no positivity was detected in urine culture, while *E. coli* and *Klebsiella oxytoca* were seen in tracheal aspirate culture.

DISCUSSION

During the COVID-19 pandemic, it was observed that there were serious decreases in the number of organ donations and family consent all over the world and in Turkey. Especially in the early stages of the pandemic, the number of organ donations and transplants has decreased worldwide, as in Turkey. In 2020, the diagnosis of brain death in our country decreased by 25% when evaluated according to the last 10 years, and 40% when evaluated compared to the previous year. Family consent rate decreased by 25% when evaluated according to the average of the last 10 years, and decreased by 50% when evaluated compared to the previous year [7].

According to the data of the Ministry of Health, 2309 patients were diagnosed with brain death in 2019 in Turkey. Six hundred nineteen family consents were obtained from 2309 patients. 2504 organs were harvested from these patients. When compared, the number of diagnosed brain death in 2020 and 2021 was 1391 and 1421, respectively, the number of family consents was 263 and 305, and the number of organs accepted for donation was 1059 and 1250, respectively [8].

In our study, 37 of our 56 patients diagnosed with brain death before the pandemic were donors, while 53 organs were recovered. During the pandemic, 21 of 39 patients became donors and 38 organs were provided. Between the two periods, there was a 30.35% decrease in the diagnosis of brain death, a 43.24% decrease in the number of donors and a 26.41% decrease in the number of organs supplied. Donations could not be received from 39 potential donors who were diagnosed with brain death during the pandemic period, because three families did not come to the meeting, two patients had a suspicion of COVID-19 and three patients were SARS-CoV-2 RT-PCR positive. Causes directly related to COVID-19 resulted in a 20.51% reduction in donors.

During the pandemic, family interviews were generally conducted by telephone around the world [9]. In a study in Israel, the first family contact was made via telephone for 18% of potential donors, and it was suggested that this negatively affected the donation process [10]. Organ transplant coordinators at our center continued face-to-face meetings, observing preventive measures against infection. The decision to donate organs is often made in complex situations. The fact that families are in the acute period, which includes the bereaved period, may prevent emotional confusion and clarity about brain death. This negatively affects family decision-making and grieving, causing distress. There are many reasons that affect family approval in organ donation. Among the various reasons for not accepting donations, he cited variants of emotional exhaustion and inadequate staff responsiveness and coping with family pain [11]. The donor rate was 63% among 56 patients with pre-pandemic diagnosis of brain death. During the pandemic, there was a decrease in both the number of brain death (n = 39) and the rate of being a donor (52.5%). It is known that the family consent rate for organ donation in Europe is between 50% and 80%, consistent with our study. These rates are lower in Asian countries due to religious beliefs and the rate of practical consent is not well known [11-13]. It is clear that innovative technological solutions need to be worked on to increase virtual interactions with family members in times of crisis such as pandemics [10].

Viral RNA samples of SARS-CoV-2, which is primarily airborne and transmitted by droplet routes, have also been detected in hepatocytes, renal tubular cells and myocardium in critically ill patients. This raises concerns that infection may be transmitted from the donor [14]. Some authors argue that as the impact of the pandemic changes, existing recommendations should be reassessed. They suggested that for patients with life-threatening organ dysfunction who are unlikely to find a suitable and timely infected match, organ transplantation from SARS-CoV-2-infected but carefully selected donors could be lifesaving for these patients [15]. Our five patients, no organ removal was

performed due to the suspicion or positivity of COVID-19.

In a study, it was observed that the most common cause of brain death was intracerebral hemorrhage (42%), followed by traumatic brain injury (343/1844, 19%) [16]. Intracranial hemorrhage was the most common cause of brain death in different studies during the COVID-19 pandemic [17, 18]. Similarly, in our study, the most common cause of brain death was intracerebral hemorrhage both in the pre-pandemic period and during the pandemic period. In the pre-pandemic period, trauma patients were in the second rank, while other intracranial events were in the second rank during the pandemic period. The reason for this is thought to be the decrease in trauma cases due to pandemic bans. In the first wave of the pandemic, this was a 4.5% reduction in donors who died from trauma, and a 25% reduction in donors who died from traffic accidents [19].

Different results have been obtained in studies examining the effect of brain death diagnosis time on family donation rate. Kıraklı *et al*. [20] reported that the definitive diagnosis period of brain death was significantly shorter in those who accepted organ donation. Researchers have suggested that the shortening of the definitive diagnosis of brain death may increase the organ transplant acceptance rate of families. Lustbader *et al*. [21] in their study, they reported that the number of donors decreases as the duration of brain death diagnosis increases, and they recommended not to waste time for a second neurological examination. In a study, cases diagnosed with brain death were divided into "early diagnosed group (diagnosed with brain death before 48 hours following ICU admission)" and "delayed diagnosis group (diagnosed after 48 hours following ICU admission)", donation rate was 73%, and 55% in those diagnosed late [11]. The time elapsed between admission to the intensive care unit and diagnosis of brain death was 115.37 ± 89.1 hours and 124.66 ± 152.68 hours before and during the pandemic, respectively. While the time between family interview and surgery was 9.33 ± 2.19 hours before the pandemic, it was found to be 15.29 ± 4.28 hours during the pandemic. We did not examine the relationship between diagnosis time and donation rate. In a study conducted in our country, the time between admission to the intensive care unit and diagnosis of brain death was found to be 4 (IQR 5) days and 4 (IQR 12) days before and during the pandemic, respectively. In the same study, the duration of organ donation was found to be 8.5 ± 2.12 hours in the pre-pandemic period and 54 ± 11.53 hours in the pandemic period [17]. In another study, the median time from admission to the intensive care unit to the diagnosis of brain death was 4 (min-max, 1.0-36.0) days during the pandemic period [18]. Balkaya *et al*. [22] found similar results with our study as the time between admission to the ICU and diagnosis of BD was 114 ± 92.8 (11-360) hours.

Infection of the donor with any pathogen causes concern in organ transplantation. Many transplant centers are not willing to harvest organs from patients with bacteremia. In contrast, some centers are carefully examining documented cases of bacteremia from potential donors who have recently received adequate antibiotic therapy. Long-term ICU stays due to additional considerations on donors potentially increase the risk of ICU-derived infections. Patients under mechanical ventilation and invasive hemodynamic monitoring should be alert to complications such as ventilator-associated pneumonia and catheter-related infection. Infection control measures, rapid screening of blood cultures and, if necessary, appropriate antibiotic therapy can reduce donor loss [17, 18]. In this study, blood, urine and tracheal aspiration samples from potential donors with brain death were conducted. During the pandemic period, the most common microorganisms were *S. haemolyticus* in blood samples, *E. coli* in urine samples, and *A. baumanii*, *B. cepacia, S. aureus* in tracheal aspirate samples. During the pandemic period, *S. haemolyticus* was the most common in blood samples, no growth was detected in urine samples, *E. coli* and *K. oxytoca* were seen in tracheal aspirate samples. When the values of the patients before the pandemic and at the time of the diagnosis of brain death were compared, CRP values of the patients were higher than at the time of the diagnosis of brain death. In another study conducted in our country, CRP elevation was found in the diagnosis of brain death [17].

As the duration of brain death diagnosis increases, the survival expectancy of patients and the stress and sadness of families increase, especially in poorly informed families. The use of supportive diagnostic tests

other than neurological examination and apnea test in the brain death diagnosis process may be effective in shortening the diagnosis period. In addition, positive communication with the family from the moment the patient is taken to the intensive care unit and providing sufficient information about the treatment steps can eliminate the negative effects on donation rates.

Limitations

There are some limitations of our study, such as being single-centered and retrospective, not investigating the characteristics of families and what influences family decisions, and not including detailed information about family interview conditions.

CONCLUSION

In this study, the organ donation process during the COVID-19 period was examined. There was a decrease of 30.35% in the diagnosis of brain death, 43.24% in the number of donors and 26.41% in the number of organs supplied. The time between family interview and surgery was significantly longer during the pandemic period. Brain death procedures should be carried out quickly due to the increased risk of infection and deterioration of the general condition.

Authors' Contribution

Study Conception: GK; Study Design: GK; Supervision: GK, FÇ; Funding: GK, FÇ; Materials: GK, FÇ; Data Collection and/or Processing: GK, FÇ; Statistical Analysis and/or Data Interpretation: GK, FÇ; Literature Review: GK, FÇ; Manuscript Preparation: GK and Critical Review: GK, FÇ.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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