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Research Article

The hidden treasure of the donor pool: An analysis of donor hearts not used as grafts

Donör havuzunun gizli hazinesi: greft olarak kullanılmayan donör kalplerinin analizi

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ABSTRACT

Aim: The aim was to investigate the course of organ donation in patients with brain death, examine the steps from organ donation to transplant, reveal the reasons of donors that are not used or are refused and to propose a solution.

Material and Methods: Between January 2015 to December 2016, we reviewed data of donor registry in Ministry of Health, Department of the National of Coordination Center archives of all cadaveric donors whose family permit approved were investigated. Data of demographics, intensive care unit data and reasons of unused as donor were analyzed.

Results: 985 donors were examined; 65% was male, mean age was 47.5 (0-96) and 65% of the donors had brain death due to neurological reasons. Mean brain death report duration was 5.4 ± 9.3 (1-169) days. A total of 169 (17.1%) infections in donors were detected. Mean intensive care unit stay was 8.55 ± 4.42 (2-38) days. Only 16.2% (159) heart grafts were used in donors. 495 (50.2%) donors were rejected for medical reasons, 64 donors (6.5%) were not eligible for heart grafts due to rejection by centers. Family approval for the heart donation was not obtained in 20% of the potential donors. 70% of donors without family approval was under 65 year-old and 67% of them did not have any medical problems for avoiding heart usage as a graft. In donors without heart approval as a graft, rate of liver use as a graft was 71% and rate for kidney was 70%.

Conclusion: We need organ transplant teams who will conduct and lead the process from the diagnosis of brain death to the care of donors.

Keywords: organ donation, heart, organ transplantation, brain death

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ÖZ

Amaç: Bu çalışmada beyin ölümü gerçekleşen hastalarda organ bağışının seyrini araştırmak, organ bağışından organ nakline kadar olan aşamaları incelemek, kullanılmayan veya reddedilen vericilerin nedenlerini ortaya çıkarmak ve çözüm önerileri ortaya konması amaçlandı.

Gereç ve Yöntemler: Ocak 2015-Aralık 2016 tarihleri arasında, aile izinleri olan tüm kadavra bağışçılarının Sağlık Bakanlığı Ulusal Koordinasyon Merkezi Başkanlığı arşivlerindeki donör kayıt verilerini inceledik. Donör adaylarının demografik verileri, yoğun bakım kalış süresindeki verileri ve donör olarak kullanılmama nedenleri incelendi.

Sonuçlar: 985 donör incelendi; %65'i erkek, ortalama yaş 47.5 (0-96) idi ve donörlerin %65'inde nörolojik nedenlerle beyin ölümü gerçekleşmişti. Ortalama beyin ölümü rapor süresi 5.4 ± 9.3 (1-169) gündü. Donörlerin 169'unda (%17.1) enfeksiyon tespit edildi. Ortalama yoğun bakımda kalış süresi 8,55 ± 4,42 (2-38) gündü. Donörlerin sadece 159'undan (%16,2) kalp grefti alındı. 495 (%50,2) donör tıbbi nedenlerle reddedildi, 64 (%6,5) donör, alıcı merkezler tarafından reddedildiği için kalp nakli için uygun değildi. Potansiyel bağışçıların %20'sinde kalp bağışı için aile onayı alınmadı. Aile onayı olmayan bağışçıların %70'i 65 yaşın altındaydı ve %67'sinin greft olarak kalp kullanımından kaçınmak için herhangi bir tıbbi sorunu yoktu. Kalp onayı olmayan donörlerde greft olarak karaciğer kullanım oranı %71, böbrek için kullanım oranı %70 idi.

Sonuç: Beyin ölümü tanısından donörlerin bakımına kadar olan süreci yürütecek ve yönlendirecek organ nakli ekiplerine ihtiyacımız vardır.

Anahtar Kelimeler: kalp nakli, beyin ölümü, donör

Introduction

Heart transplantation remains the most crucial treatment option for patients with end-stage heart failure (HF) despite advancements in medical treatments and mechanical support devices. Unfortunately, there is a mismatch between the number of donors and recipients, leading to a steady increase in the number of patients on the waiting list, prolonging wait times, and resulting in more deaths. According to data from the Ministry of Health in Turkey, the number of patients awaiting heart transplantation was 1016 in 2018. In the last six years, an average of 72 heart transplants were performed annually in Turkey, and the average waiting time for heart transplantation is approximately eight months (1).

In many countries, ongoing studies focus on strategies to increase the number of donors. National guidelines define marginal donors to maximize the benefit from donors, and significant efforts are made to enhance organ utilization (2). Despite a two-fold increase in the detection of brain death in recent years through collaboration between the Turkish Ministry of Health and other institutions, the number of heart transplants has not seen a proportional rise, with only 7-10% of patients on the waiting list able to undergo heart transplantation (1). Ensuring proper care for donors and obtaining family approval are critical factors to prevent shortcomings in maximizing organ usage. Despite clinical guidelines for donor care, organ donation rates vary (3-6). While high donation rates indicate success in donor care, the key factor in boosting organ donation lies in effectively managing the family consent process. Therefore, organ donation necessitates an approach that considers all steps to yield more effective results (7).

The aim of this study is to assess the stages of organ donation, understand the reasons for the refusal of grafts, and provide recommendations to enhance the utilization rate of donor organs.

Material and Methods

Patients and Data Collection

In Turkey, donor and transport centers operate under the jurisdiction of the Regional Coordination Center (RCC). The RCC is affiliated with the National Coordination Center (NCC), a division of the Ministry of Health. Donor data is submitted to the RCC, and subsequently, all potential heart grafts undergo evaluation by the scientific committee in the NCC. Suitable grafts are then presented to transplant centers through the NCC, while grafts deemed unsuitable for medical reasons (GNSMR) are not presented to transplant centers. The regulatory framework for organ transplantation is outlined in Figure 1.

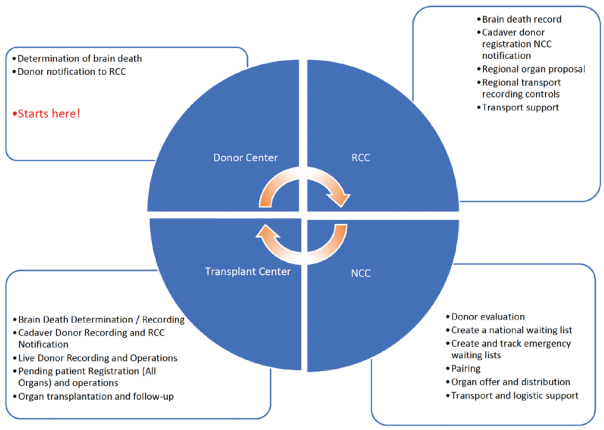

Figure 1. Organizations and Tasks in Organ Transport.

The study population comprised donor reports of all cadaveric donors who obtained family permits between January 2015 and December 2016, as recorded in the NCC archives, given that permission could be obtained within the specified timeframe.

Demographic data: RCC in charge, age, blood type, cause of death, gender, weight, height.

Patients history: Diseases, medications, smoking history, drug abuse and alcohol use, previous surgery.

Transplantation data: which organs were used, organ the family did not want to donate, decline for cardiac graft, GNSMR, absence of match with recipient, recipient city and transplant centers of used hearts.

Data on intensive care follow-up: intensive care unit (ICU) time to brain death, duration of mechanical ventilation, respiratory or cardiac arrest, central venous pressure (CVP), blood pressures, medications and inotropic agents. The time from the occurrence of brain death to notification to the NCC is defined as brain death notification time.

Interview with family: After the diagnosis of brain death in the donor center, family interviews were conducted by the transplant coordinator nurse and the responsible physicians.

Laboratory data: Hemogram and biochemical parameters, viral markers, echocardiographic evaluations, infection status and culture evaluations.

Organ Refusal Criteria: Based on the guidelines of the International Society for Heart and Lung Transplantation(8);

• High inotrope: dopamine above 20 mcg / kg / min

• Prolonged ischemia time: 4 hours and above

• Low ejection fraction (EF): 40% and less.

Study permissions: Written approvals were obtained from local ethical committee. A protocol was signed between our center and the Ministry of Health of Turkey and necessary permissions were obtained.

Statistics

Data were analyzed by SPSS for Windows 21 (SPSS Inc. Chicago IL, USA). The Kolmogorov-Smirnov test was used to determine whether the distribution of continuous numerical variables was normal distribution. Descriptive statistics were shown as mean±standard deviation or median (minimum-maximum) for continuous numerical variables; number of cases and (%) for categorical variables. The significance of the difference between the groups in terms of median values was examined by Mann Whitney U test. Categorical variables were evaluated by Pearson's chi-square, Fischer's exact or likelihood ratio test. Results for $p < 0.05$ were considered statistically significant.

Results

Donor Pool

Number of brain deaths were found to be 3987 (Figure 2). Data of 985 (24.7%) donors with family approval were evaluated. The demographic characteristics of the donors are summarized in Table 1. The mean age was 47.5±21.3(0-96) years and 65% of the donors were male. The major cause of brain death was neurological events (69%) (Table 2). The mean brain death notification time was 5.4 ± 9.3 (1-169) days. 84% of donors received at least one positive inotropic agent (57% received one or more positive inotropes at high doses).

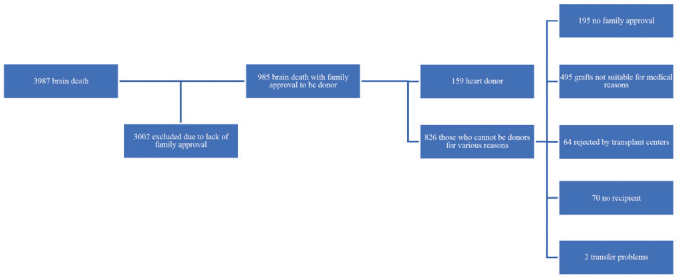

Figure 2. Flowchart for donor evaluation.

Of all donors, 169 (17.2%) had evidence of a clinically diagnosed infection. The most frequent micro-organism isolated from blood culture was Staphylococcus aureus whereas Acinetobacter baumanii was the most frequent micro-organism isolated from deep tracheal aspirate. The mean duration of ICU stay in patients with infection was 8.55±4.42 (2-38) days.

Table 1: Demographics Data of Donors, n=985.	
Gender	n (%)
Female	353 (%35)
Male	632 (%65)
Age (mean±SD years)	47,5±21,3
0-1	14 (%1)
1-17	110 (%11)
18-50	502 (%51)
51-64	250 (%25.3)
≥65	234 (%23)
Weight (mean±SD kg)	72,7±19,1
Height (mean±SD cm)	165,8±20,4
Co-morbidity	
Cardiac history	110 (%11)
Diabetes mellitus	101 (%10)
Chronic obstructive pulmonary disease	32 (%3)
Thyroid dysfunction	20 (%2)
Hypertension	197 (%20)
Active smoking	340 (%34)
Alcoholism	37 (%4)
Drug abuse	11 (%1)
A Rh+	374 (38,0%)
0 Rh+	311 (31,6%)
B Rh+	153 (15,5%)
AB Rh+	61 (6,2%)
A Rh-	51 (5,2%)
0 Rh-	21(2,1%)
B Rh-	9 (0,9%)
AB Rh-	3 (0,3%)

Table 2: Causes of brain death		
Definition	Comment	n (%)
1. Group Neurological events	Isolated central nervous system events, spontaneous intracranial hemorrhage, cerebrovascular events, etc.	647 (66%)
2. Group Trauma	Traffic accident, isolated head trauma, falling, gun-shot injury, penetrating stab wounds, etc.	200 (20%)
3. Group Cardiopulmonary events	Coronary artery disease, myocar-dial infarction, foreign body aspi-ration, drowning, pulmonary thromboembolism, etc.	65 (7%)
4. Group Systemic diseases	Malignity, metabolic diseases, intoxication, infections, etc.	61 (6%)
5. Group Suicide	-	12 (1%)

Unused Heart Graft Analysis

Of 985 donors, only 159 (16%) was accepted as a heart donor; 826 (84%) donors could not be evaluated for organ transplantation due to various reasons (Table 3).

Table 3: Evaluation of unused hearts (n=826)	
	n(%)
1. No family approval	195 (%23.7)
• 0-17 years	17
• 18-54 years	73
• 55-64 years	59
• 65 years and above	46
2. Grafts not suitable for medical reasons (GNSMR)	495 (%60)
• Cardiac issues	95
• Old age	193
• Infection	62
• Prolonged CPR / High inotropes	72
• Other	73
3. Rejected by transplant centers	64 (%7.7)
• Rejected intraoperatively	32
• Older age	10
• Infection	10
• Other causes	7
• Prolonged CPR/high inotropes	4
• Low cardiac performance	1
4. No recipient	70 (%8.4)
5. Transfer problems	2 (%0.2)
CPR: Cardiopulmonary resuscitation	

a) Family Refused Donors

Family approval was not obtained for the use of heart graft in 195 (23.7%) donors (76.4% of these donors were under 65 years of age) (Table 4). In this group, where cardiac donation was not approved by the family, it was observed that there were approvals of liver, kidney and/or lung transplant and appropriate organs were used (Table 4).

Table 4: The state of approval and using of other organs of the family without cardiac donor approval	
Organ	Approval/Used (n/n)
Liver	177/140
• Kidney	169/137
• Lung	18/1

b) Grafts not suitable for medical reasons

Four hundred and ninety five (60%) donor's heart graft was evaluated as GNSMR. The most common cause of GNSMR was advanced age (39%) and cardiac issues (19%) (Table 3).

c) Rejected by Transplant Centers

Transplant centers rejected 64 (7.7%) potential donors and 50% of cardiac grafts were refused intraoperatively after sternotomy (Table 3). The most common reason for rejection of organ use was the detection of plaque in coronary arteries. Pericardial adhesion was observed in two donors, cardiac contusion was thought to be related to cardiopulmonary resuscitation (CPR) in two donors, and size mismatch was observed in two patients. The mean age of the rejection due to older age group was 61.8 ± 4.7 (54-66) years.

d) No Recipients

Seventy potential heart donors could not be used due to the lack of suitable recipients (Table 3)

e) Transfer problems

Two (0.2%) donor hearts were not used due to weather condition (Table 3).

Discussion

To achieve an adequate donor supply, increasing the number of brain death detections and obtaining family permissions are crucial. According to the International Registry in Organ Donation and Transplantation (IRODAT) report between 2015 and 2016, Turkey leads with 45.7 live donors per million population, but lags behind in cadaveric donors with 7.20 per million, ranking 46th globally (9). In our study, we examined the entire donor pool and identified potential usability, especially in grafts that were not cardiac donors.

Only 25% of 3987 brain deaths were given family consent and, only 4% of all donors with brain death was accepted as heart donor, in our study. Furthermore, 63% of donors without family permission were under 65 years of age. Although the rate of obtaining family consent after notification of brain death in Europe varies between countries, it appears to be above 60% in most countries. In the case of organ donations and cadaver donor procurement; family rejection rates in 2016 were; 30% in Italy, 25% in Lithuania, 10% in Croatia, 13% in Spain, 10% in Belgium, and 75% in Turkey (79.5% for heart) (11). In Turkey, according to Ministry of Health data(12) between the years of 2011-2017, number of brain death was increased, however, donation rate remained stagnant(1). Interestingly, families who did not give permission for cardiac donors were found to be able to consent to the use of other organs. Turkey's sociocultural status and religious beliefs may be the reason for the family refusal. In a retrospective study from Iran, one of the major Muslim countries, the most common reasons for family rejection were; denial of patient death and distrust of diagnosis (44%), belief that brain death is a miracle (14%), not conforming to religion (13%) and organ trade (10%) (13). Although the ministry of religious affairs in Turkey says that organ donation is not contrary to Islamic religion. In the study of Kirakli et al.(14), religious reasons were shown as the highest cause in the group who were not approved for organ donation from patients diagnosed with brain death.

To increase organ donation, the organization of health workers is as important as raising awareness in the society. In Spain, highest rank in organ donation, a system has been running by the National Transplant Organization (ONT) under the Ministry of Health, since 1989. The transplant donor coordinators are all specialist clinicians supported by coordinator nurses(15). These teams have primary responsibilities such as recognizing, tracking and informing donor candidates in the region where they work. Thus, lesser number of brain death diagnosis has been missed out and the number of organs used has increased(16). In Croatia, there has been a high momentum in organ donation in the last 10 years, where intensive care professionals working as donor coordinators received additional training on donor recognition and management (17).There are also specialized physicians who provide 24-hour support in the relevant health ministry, which also helps in pursuing the necessary medical support and accelerating the process. In both countries, it has been reported that it is important to support the health ministries both by civil society organizations and religious communities. In Turkey, the organ coordinators are certified by the Ministry of Health after training for a certain period of time. However, the professionalization of the people working in this field will ensure the detection of brain death is accurate and earlier.

The time to detect brain death in our country was longer than other developed countries. Donor care team may shorten the time of brain death by regular ICU visits and interviews with responsible physicians and avoid hemodynamic instability and donor infection due to delay.

Lustbader et al.(18) reported prolongation of brain death reporting period reduced both the rates of organ use and family approvals. In a meta-analysis of Sandorini et al.(19), the mean duration of brain death of 1830 patients was 5.4 ± 9.3 (1-169) days and the prolongation of the duration of ICU stay was expected to increase the rate of infection. In our study, no significant difference was found between the duration of hospitalization for donors who were proved to be infected

and those who were not. In donor care, Staphylococcal strains isolated from blood cultures were thought to be associated with donor skin contamination. Acinetobacter was the most produced bacteria in donor deep tracheal aspirate cultures. The reason for this situation is thought to be endemic in Turkey.

In donor evaluation, comorbidities are very important in decision making. In our study, cardiac history and older age were the most important factors for donor to be GNSMR. Neurological events were very prominent cause of donor death in our study, while trauma was the primary cause in other studies(20). As the standard donor criteria do not meet the need for increased heart transplantation, this discrepancy between the number of donors and recipients leads to a steady increase in the number of patients in the waiting list, prolonging the waiting period and increasing deaths. In some countries, approximately 50% of the patients in the waiting list cannot undergo heart transplant due to long waiting period and inadequate organ donation(21). Therefore, modified protocols have been published over the past 25 years regarding the appropriateness of potential heart donors(21-23). In many countries, marginal donor definitions were made according to national guidelines and they tried to maximize organ use(24, 25). In a multicenter retrospective study by Fiorelli et al.(26), involving 512 heart transplant patients, 134 (26%) reported that the donor was infected, and 40 donors had diabetes mellitus and they found that infection did not affect survival. In a meta-analysis by Joseph et al.(27) in which they examined 5342 heart transplants via UNOS data, they reported heart use from hyperglycemic donors did not make a significant difference in long-term survival.

If the family permits for other organs could also be taken for the heart, and the donor care could be taken more carefully, the number of heart transplants in our country between 2015-2016 would have doubled. Considering the clinical status and urgency status of the recipient candidates waiting list in the transplant centers, the approach to a determined donor may differ. The necessity of utilizing marginal donors becomes prominent in this context. Donor hearts, even if approved by the scientific committee, might face challenges arising from donor management or the donor's own hemodynamic issues until the evaluation on the operating table. In this context, the visual assessment of the donor heart becomes crucial. Furthermore, scientific boards can deliver presentations to transplantation centers advocating for the utilization of marginal donors.

Limitations

There are several limitations of our investigation, the first of which is its retrospective, observational nature. In addition, the study was carried out on the basis of donor reports. Laboratory findings, clinical features, echocardiographic evaluations whose records may be missing in the NCC archives. The reasons for not giving consent in the group with no family approval could not be investigated especially in patients with brain death.

Conclusion

In this study, detection of brain death in our country has increased over the years, however, usage of cardiac grafts has not met the increased need to catch up the growing waiting list substantially due to insufficient family approval. It is very important to provide informative training on organ donation and increase social awareness. In addition, it is essential that health workers who will conduct family interviews are subject to a separate training program. In the process of donor detection and organ transplantation, transplant coordinators should carry more efficient work out, especially with regard to potential donor detection and care. The donors should be monitored regarding their brain death assessment, detection, notification, organ distribution and inferences during their follow-up in ICUs. By contributing remote donor care and consultancy, number of suitable grafts can be increased by creating a 24-hour expert staff within the Ministry of Health. We believe that transplant waiting lists need to be rearranged to increase the number of heart transplants, and in particular to reduce the number of pending patients in risky recipient groups.

Conflict of Interest

None.

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