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A Single-Center Experience with an Intensivist-Led Brain-Dead Donor Management Program

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Background: The aim of this study is to report our experience of brain-dead donor management by a dedicated intensivist who had wide experience in treatment of hemodynamically unstable patient and to suggest a role for intensivists in organ donation.

Material/Methods: The management of brain-dead donors was performed by experienced intensivists. The hospital medical records and data from the Korean Network of Organ Sharing from August 2013 to December 2016 were reviewed retrospectively.

Results: Fifty-four brain death patients (3.2% of KONOS nationwide data) donated organs in our institution during 41 months. Dedicated intensivists managed deceased patients for the whole duration (2.81 ± 1.21 days) of management, not only with conservative therapies like fluid resuscitation, vasopressor, or hormonal replacement, but also with pulmonary artery catheter insertion for cardiac output monitoring ($n=47$, 87.0%) and continuous renal replacement therapy ($n=22$, 40.7%). The number of donors increased each year. The mean number of retrieved organs in each deceased donor was 3.98 ± 1.55 , more than the national average (3.26) and comparable to the higher level among the recent worldwide data. The number of donations by organ was: 23 hearts (4.9% of nationwide data), 17 lungs (7.5% of nationwide data), 102 kidneys (3.3% of nationwide data), 47 livers (3.1% of nationwide data), 6 pancreases (2.9% of nationwide data), 1 pancreatic duct (11.1% of nationwide data), and 1 small intestine (12.5% of nationwide data).

Conclusions: Management by dedicated intensivists will improve not only the number of actual organ donors, but also the number of harvested organs.

MeSH Keywords: Brain Death • Intensive Care • Organ Transplantation • Tissue and Organ Procurement

Full-text PDF: <https://www.annalsoftransplantation.com/abstract/index/idArt/912025>



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Background

Transplant surgery is the ultimate and the only treatment for end-stage organ failure patients [1–3]. The number of patients waiting for transplants shows an increasing tendency worldwide. In fact, the total number of people waiting for transplants in the United States was 83 731 in 2003, but the number has increased steadily over the years, reaching 122 071 in 2015 [4,5]. In Korea, the number of patients waiting for transplants (excluding tissue transplants) was 2840 in 2000 and increased to 24 611 in 2016, showing a 766.6% increase [6].

The number of transplant surgeries performed is small compared with the number of people waiting for organ transplantation around the world. In the United States, 122 071 people awaited transplant surgery in 2015, but only 30 975 transplants were performed, of which about 24 980 transplanted organs were obtained from deceased donors [4,5]. In Korea, 24 611 people were registered on transplant wait lists during the year 2016, and 4528 transplants were actually performed, of which 2319 organs were obtained from 573 brain death donations [6]. As can be seen from these statistics, the shortage of organ donation is a serious problem worldwide. Therefore, new attempts are being made to acquire organs from marginal donors by extending donation criteria, enabling transplantation from new donation sources, or to increase the number of available organs per donor by active and aggressive brain death management.

Brain death refers to irreversible cessation of whole brain function in which the body is unresponsive to all stimuli and has no movement, including breathing [2,7]. The recognition of brain death enabled the activation of organ transplantation; however, brain-dead donors and deceased donors are both in hemodynamically unstable and pro-inflammatory states. In particular, brain-dead donors continue to have cardiovascular and physiologic instability due to catecholamine surge, central sympatholysis, and hormonal dysregulation [8,9]. These hemodynamic, endocrine, and metabolic imbalances lead to multiple organ failure, resulting in cardiovascular failure occurring in about 60% of potential brain deaths [10], and about 25% of potential brain-dead patients have been reported to die despite treatment [11]. In addition, this series of changes can affect the function and prognosis of transplanted organs [8]. Therefore, careful and professional management is required. Dedicated intensivists usually have enough experience in the management of hemodynamically unstable patients like brain-dead donors to perform the required management for organ donation.

By analyzing our institution's experience with brain-dead donor management by intensivists, we here aim to suggest a role for intensivists for organ donations and transplantations.

Material and Methods

Patients

Ewha Womans University Medical Center (EUMC) is a tertiary hospital in Seoul, South Korea, with about 800 beds, of which 54 are in its 4 intensive care units (ICUs). A certified intensivist was hired in the ICU of EUMC in March 2013. Soon thereafter, EUMC signed a memorandum of understanding (MOU) with the Korean Organ Donation Agency (KODA) and started an organ donation campaign. The management of deceased donors was performed by experienced intensivists. In South Korea, there were a total of 95 institutions that managed brain-dead donors in cooperation with KODA in 2016.

Outline of EUMC brain-dead donor management

In Korea, the government intervenes in the management of brain-dead organ donors, and only an authorized institution can perform this role. EUMC could not manage brain-dead donors until it obtained approval from the government. Therefore, suspected brain-dead patients who had expressed the intention to donate their organs had been referred to other authorized hospitals. Before transferring patients to other hospitals, extremely limited conservative treatments were performed by attending physicians of admitting departments without any special protocols, performing basic monitoring of vital signs, preservation of controlled mode of mechanical ventilation, and minimal fluid administration without nutrient support.

After an experienced intensivist acquired a new position, EUMC started brain-dead donor management after obtaining qualification on March 2013. Once a suspected brain-dead donor was found, the patient was referred to the brain death management team. Then, responsible intensivists dedicated themselves to the care of that donor for 24 h during the course of management and cared for the donor intensively, following the prescribed protocol (described below). After transferring the patient from the ICU to the operating room for organ recovery, anesthesiologists in charge of transplantation surgery assumed the responsibilities and cared for the donors.

Protocol EUMC brain death management

The brain death management protocol of our institution is as follows. Organ donors whose organ donation has been determined first stop all treatments for brain protection, instead receiving treatment for organ saving and protection. These organ-protection treatments include: (a) pulmonary artery catheterization and central venous catheterization for hemodynamic monitoring and fluid resuscitation; (b) aggressive fluid challenge and resuscitation when evidence of fluid depletion (e.g., low blood pressure, high pulse, increased lactic acid, decreased

venous oxygen saturation, small left ventricle size in echocardiography, small diameter of inferior vena cava) are verified; (c) use of an appropriate vasopressor if low blood pressure with inadequate tissue perfusion has been continued despite fluid resuscitation; (d) in cases of central diabetes insipidus due to inappropriate releasing of vasopressin is suspected, continuous vasopressin infusion; (e) if hormonal insufficiency other than vasopressin is expected, corticosteroid hormone and thyroid hormone replacement; (f) continuous renal replacement therapy (CRRT) if there is suspicion of acute kidney injury (AKI) [12]; with oliguria that does not respond to fluid resuscitation or suspected severe uncontrolled severe metabolic acidosis or lactic acidosis; (g) if a large amount of pleural effusion is found, insertion of a percutaneous drainage catheter to prevent passive atelectasis and perform lung recruitment, along with toiletting through bed-side bronchoscopy to ensure lung care; (h) possible enteral tube feeding to maintain intestine mucosal integrity; and (i) during apnea test, oxygen supplied by cannula connected to bag valve mask (Ambu® bag) with positive end-expiratory pressure (PEEP) valve to prevent decruitment of lungs after pre-oxygenated with 100% O₂ for 10 min [13].

Data and statistical analysis

Among a total of 151 cases of potential brain deaths, we studied 54 cases of actual donors who donated organs from August 2013 to December 2016 in our institution. The hospital medical records of these deceased donors and the data of the Korean Network of Organ Sharing (KONOS) from August 2013 to December 2016 were reviewed retrospectively.

Data were analyzed using IBM SPSS version 20.0 (SPSS® Inc., Chicago, IL). Numerical data, such as age or the number of donated organs, are represented as mean ± standard deviation, and data about patient characteristics and univariate analysis of influencing factors were analyzed with the χ^2 test and Fisher's exact test. We considered *p* values less than 0.05 to be statistically significant.

This study was approved by the Institutional Review Board (IRB) of EUMC (IRB number, EUMC 2017-02-016).

Results

A total of 151 potential brain deaths were reported to KODA during the 41 months from August 2013 to December 2016. Of these, guardians of 58 brain-dead patients agreed to donate organs, of which 54 finally donated organs. Of 4 patients who agreed to organ donation but did not achieve it, the brain death managements were terminated in 2 patients because there were no recipients due to old age and active hepatitis C viral infection. One patient was found not to be brain dead

Table 1. Demographic characteristics of brain death donors.

Variables	
Age (years)	44.7±15.9
Sex	Male: Female=2: 1
Body mass index	22.9±4.0
APACHE II score (points)	30.5±7.2
Acute kidney injury	22 (40.7%)
Interval from admission to organ donation (days)	11.59±17.74
Duration of brain death management (days)	2.81±1.21
Number of procured organs	3.98±1.55

APACHE – acute physiology and chronic health evaluation.

during primary brain death examination. The other patient underwent extracorporeal membrane oxygenation (ECMO) therapy due to cardiac arrest during brain death management, and an emergent laparotomy was performed to obtain organs; however, donation could not be accomplished due to hypoperfusion of organs, and the patient died.

Demographic characteristics of the 54 brain-dead donors are shown in Table 1 and Figure 1. There were no significant differences between the brain-dead patients who provided consent for organ donation from the guardians and those who did not (Figure 1). The mean period from admission with primary disease to the report as a potential brain death was 6.28±13.63 days (range 0–85 days), and the time from the report to the KODA to obtaining the donation consent from guardians was 1.69±2.70 days (range 0–14 days). The mean duration of brain death management after transfer to the brain death management team was 2.81±1.21 days (range 2–9 days), and the intensivists dedicated themselves to care for the donor for the whole duration of management (Table 1). We performed pulmonary artery catheter insertion in 47 patients (87%). During brain death management, 4780.54±2668.54 mL (range 860–12 434 mL) was administered for 24 h right after the transfer (Table 2).

We performed a modified apnea test in 53.7% of patients to prevent lung decruitment during brain death. We managed most of the brain-dead patients, not only with conventional therapies like fluid resuscitation, vasopressor, or hormonal replacement, but also with pulmonary artery catheterization for cardiac output monitoring (*n*=47, 87.0%) and CRRT (*n*=22, 40.7%) (Table 2).

The most common cause of brain death was cerebrovascular accident, such as spontaneous brain hemorrhage (*n*=14, 25.9%), followed by hanging-induced hypoxic brain injury

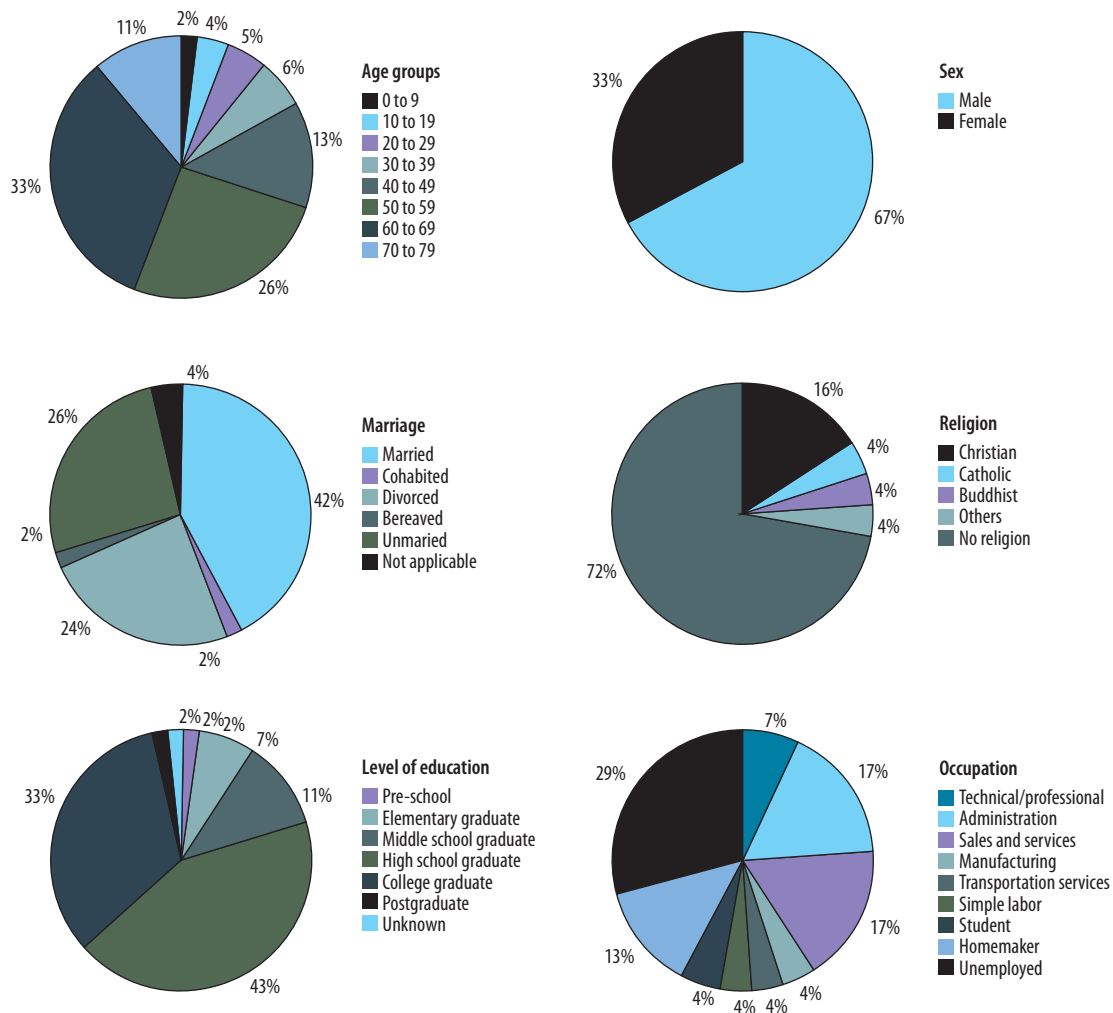


Figure 1. Demographic characteristics of brain-dead donors in EUMC. There were no significant differences between the potential-dead patients who provided consent for organ donation from the guardians and those who did not.

($n=13$, 24.1%) and cardiac arrest – induced hypoxic brain injury ($n=12$, 22.2%) (Table 3).

Fifty-four brain-dead patients (3.2% of KONOS nationwide data) donated organs in our institution, and the number of donors increased each year: there were 4 donors (2.4% of KONOS nationwide data) in 2013, 13 donors (2.9% of KONOS nationwide data) in 2014, 19 donors (3.8% of KONOS nationwide data) in 2015, and 18 donors (3.1% of KONOS nationwide data) in 2016 (Table 4) [6]. The number of donations by organ was as follows: 13 hearts (4.9% of KONOS nationwide data), 17 lungs (7.5% of KONOS nationwide data), 102 kidneys (3.3% of KONOS nationwide data), 47 livers (3.1% of KONOS nationwide data), 6 pancreases (2.9% of KONOS nationwide data), 1 pancreatic duct (11.1% of KONOS nationwide data), and 1 small intestine (12.5% of KONOS nationwide data; Table 4) [6].

The mean number of recovered organs in each deceased donor was 3.98 ± 1.55 , which was more than the national average (3.2 in KONOS nationwide data) [5] and comparable with the higher level among recent worldwide data (Figure 2) [14].

Discussion

Commonly, organs for transplantation are obtained from deceased donors. However, many Asian countries have a low deceased organ donation rate; therefore, they have an abnormal structure that relies heavily on living organ donation. Also, in some countries, including Korea, organ donation after cardiac death is not approved or activated, so brain death organ donation should be encouraged. Therefore, much effort has been made to solve these problems. First, marginal patients

Table 2. Clinical characteristics of brain death donors.

Variables	
Modified apnea test	29 (53.7%)
Fluid administration	
Fluid administration, 1 st day (mL)	4780.5±2668.2
Fluid administration, 2 nd day (mL)	6080.4±2631.4
Vasopressors	
Vasopressin	38 (70.4%)
Norepinephrine	51 (94.4%)
Epinephrine	2 (3.7%)
Dobutamine	10 (18.5%)
Dopamine	1 (1.9%)
Steroid replacement	26 (48.1%)
Pulmonary arterial catheterization	47 (87.0%)
Continuous renal replacement therapy	22 (40.7%)
Percutaneous drainage catheter insertion	15 (27.8%)

Table 3. Cause of brain death.

Causes	n (%)
Cerebrovascular accident	14 (25.9%)
Hanging-induced hypoxic brain injury	13 (24.1%)
Cardiac arrest-induced hypoxic brain injury	11 (20.4%)
Traumatic brain injury	9 (16.7%)
Stroke	2 (3.7%)
Near drawn-induced hypoxic brain injury	2 (3.7%)
Neonate hypoxic brain damage	1 (1.9%)
Others	2 (3.7%)

Table 4. Annual changes of actual brain death donors in EUMC.

		Total	2013.8~	2014	2015	2016
Brain death	KONOS	1686	166	446	501	573
	EUMC	54 (3.2%)	4 (2.4%)	13 (2.9%)	19 (3.8%)	18 (3.1%)
Heart	KONOS	472	53	118	145	156
	EUMC	23 (4.9%)	4 (7.5%)	6 (5.1%)	7 (4.8%)	6 (3.8%)
Lung	KONOS	226	18	55	64	89
	EUMC	17 (7.5%)	2 (11.1%)	2 (3.6%)	8 (12.5%)	5 (5.6%)
Kidney	KONOS	3072	304	808	901	1059
	EUMC	102 (3.3%)	8 (2.6%)	24 (3.0%)	38 (4.2%)	32 (3.0%)
Liver	KONOS	1517	149	404	456	508
	EUMC	47 (3.1%)	4 (2.7%)	12 (3.0%)	16 (3.5%)	15 (3.0%)
Pancreas	KONOS	207	21	55	57	74
	EUMC	6 (2.9%)	1 (4.8%)	1 (1.8%)	2 (3.5%)	2 (2.7%)
Pancreatic duct	KONOS	9	3	0	4	2
	EUMC	1 (11.1%)	0	0	1 (25%)	0
Small intestine	KONOS	8	2	5	1	0
	EUMC	1 (12.5%)	0	1 (20%)	0	0

KONOS – Korea Network for Organ Sharing; EUMC – Ewha Womans University Medical Center; (%) – portion of KONOS nationwide data.

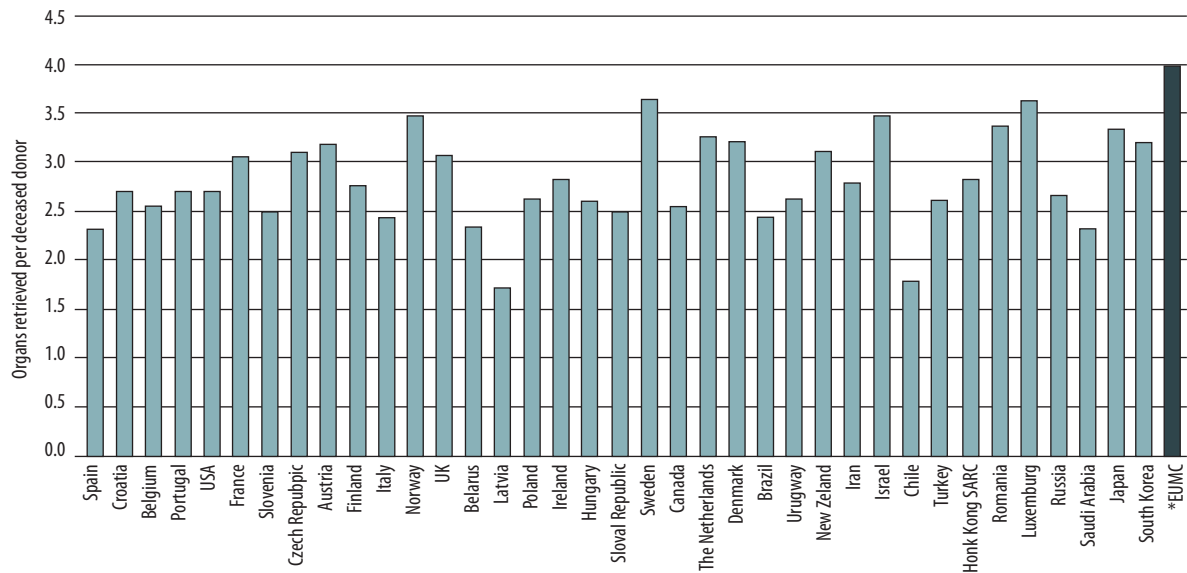


Figure 2. The mean number of organs recovered from 1 deceased donor. The mean number of procured organs were relatively higher than Korean national data, and even higher than the average of other countries. * Ewha Womans University Medical Center.

with extended criteria, from whom we had not procured organs before, have been actively considered as donors [15]. Additionally, physicians have tried to increase the number of available organs per donor by active and aggressive brain death management.

Experienced intensivists in critical care management are well aware of the physiologic abnormality of brain-dead donors, so they can increase the rate of donation of each donor using critical management, which is expected to improve the number of procured organs per donor. As mentioned earlier, 25% of brain-dead patients die during treatment in the hospital [11]; however, only 1 of our 58 patients died, who underwent ECMO in our institution.

In March of 2013, the intensivist proceeded to her new post at our institution and started the brain death management program in August of the same year. Until then, brain death patients were transferred to other hospitals capable of brain death management without any management protocols. However, in our institution, the number of actual donors increased after appointment of an intensivist as a dedicated brain death coordinator.

There are no standard international guidelines for the determination of brain death and management of potential brain deaths for organ donation; however, the following donor management goals (DMGs) have been suggested to maintain hemodynamic stability in the management of brain death and to maintain optimization of transplanted organ function: (a) mean

arterial pressure: 60–110 mmHg; (b) central venous pressure: 4–12 mmHg; (c) ejection fraction: $\geq 50\%$; (d) the number of low-dose vasopressors: ≤ 1 , (e) pH in arterial blood gas analysis: 7.3–7.5; (f) ratio of fraction of inspired oxygen (FiO_2) to partial pressure of oxygen (PaO_2): ≥ 300 ; (g) serum sodium level: ≤ 155 mEq/L; (h) urine output: ≥ 0.5 mL/kg/h over 4 hours; and (i) glucose level: ≤ 150 mg/dL [16]. A critical care management treatment strategy has been recommended to achieve these DMGs [17]. Therefore, our institution created the ‘Guideline for the Management of Brain Death’, which is based on critical care medicine with an appropriate understanding of the pathophysiology of brain deaths. Potential brain-dead donors in our institution are managed in accordance with the guideline.

In our institution, if a brain death occurs, we first perform intensive hemodynamic monitoring by inserting a pulmonary artery catheter and central venous catheter according to our protocol, and we actively administer aggressive fluid resuscitation. We performed pulmonary artery catheter insertion in 87% of patients with the administration of 4780.54 mL of crystalloid fluid for the first 24 h. Therefore, the dose of norepinephrine could be tapered off after fluid resuscitation, and only 40.7% of patients had to maintain norepinephrine infusion just before the organ procurement (Table 2). Massive fluid resuscitation under the cardiac output monitoring with pulmonary artery catheter would help to taper the vasopressor.

At the time of transfer to the brain death management team, 22 patients (40.7%) had suspected AKI. In patients who showed insufficient urinary output or sustained metabolic abnormality,

CRRT was performed at an early stage. CRRT was performed in 22 patients (40.7%), and 21 brain-dead donors were able to donate kidneys despite AKI (Table 2). We believe that CRRT at an early stage of AKI would improve not only the donation rate of kidneys, but also the function of donated kidneys.

A modified apnea test was performed in our institution. Use of an Ambu® bag with PEEP valve could be helpful to prevent the decruitment of lungs and result in the accomplishment of the apnea test without compromising safety due to hypoxia [13]. We also performed lung recruitment to improve the possibility of lung donation.

Since the onset of brain death management, we achieved 23 heart donations (4.9%), 34 lung donations (from 17 donors; 7.5%) over a period of about 41 months (Table 4). These numbers were 4.9% and 7.5%, respectively, of the organs obtained from brain deaths managed by 95 institutions in the same period. In addition, the number of procured organs per donor was 3.98 ± 1.55 , which is higher than Korea's average of 3.26. It is also comparable to other countries worldwide (Figure 2).

Because of the shortage of intensivists, they must also attend critically ill patients in the ICU when there are no donors. However, once a suspicious brain-dead donor was found, responsible intensivists dedicated themselves to care for that donor for the whole duration of management, even with changing shifts. It can be a laborious system; however, our staff in the Department of Critical Care Medicine, who have diverse backgrounds, such as anesthesiology, emergency medicine, neurology, pulmonology, and surgery, have a firm conviction that adequate management of donors by intensivists can increase the quality and quantity of organ transplantation.

It is difficult to analyze precisely the factors that led to the high proportion of heart and lung donation in our institute, but we believe that it was helpful to aggressively treat the brain-dead donors according to the criteria of critically ill patients. The most important factor allowing these relatively good

outcomes was, we believe, the management of brain death by a certified intensivist.

This study reports on the initial performance of a brain death management program at a single institution that started brain death management after appointing an intensivist. It was therefore not possible to show significance by comparison with a control group. This is a limitation of the present study because it is not possible to show how aggressive treatment by an intensivist can improve treatment results compared with other treatment conditions. However, we think it is meaningful to be able to present favorable results of the initial performance of a single institution. If the opportunity is available, multi-center studies should be conducted to provide standardized guidelines for the management of brain death.

Conclusions

It is clear that national support is needed for the improvement of institutional and domestic organ transplants. However, even in institutions or organizations with no experience of brain death management, certified intensivists are able to lead the management of brain-dead organ donors and to increase the number of procured organs.

The shortage of donated organs has been a serious issue around the world. Dedicated intensivists are important for brain death donor management through active and aggressive management with fluid challenge and adequate usage of vasopressor under the cardiac output monitoring, early CRRT, and modified apnea test and lung recruitment. Such management can improve the number of actual organ donors and recovered organs.

Conflicts of interest

None.

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