RESEARCH ARTICLE

Donor Assessment and Management System for Maximizing Heart Availability in Japan

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Abstract

As donor shortage is extremely severe in Japan because of the very strict Organ Transplantation Act, special strategies for maximizing organ transplant opportunities should be established. Since November in 2002, special transplant management doctors were sent to donor hospitals in order to assess donor's organ function and to identify which organ could be transplanted. They also intensively cared for the donor to stabilize hemodynamics and to improve cardiac and lung function by intravenously giving anti-diuretic hormone and pulmonary toileting by broncho-fiberscope. Out of a consecutive 384 brain dead donors, 284 (74.0%) donor hearts were transplanted and the patient survival after heart transplantation at 5, 10 and 15 years were 92.7, 89.6 and 81.8 %, respectively in Japan. These strategies may increase heart availability and improve post-transplant outcomes.

1. Introduction

Heart transplantation (HTx) represents established treatment for patients with end-stage heart failure and results in satisfying long-term results. However, these surgical therapies are continuously limited by severe donor organ shortage in the last years. Therefore, adequate and optimal utilization of all suitable donor hearts is mandatory to increase graft availability.

As the Japanese Organ Transplantation Act for brain dead (BD) organ donation (the former Act) issued in October 1997[1] required a living written consent for BD and organ donation, only 81 BD organ donations have been performed in entire Japan for 13 years since the former Act was issued. These great pressures of organ shortage and long waiting time had made Japanese transplant programs consider the use of donor hearts that would be considered marginal. The most troublesome issue facing HTx is the phenomenon of primary allograft dysfunction (PGD). The use of marginal donor hearts may increase the rate of PGF. From this point of view, it is necessary to establish special donor evaluation and management system to maximize donor heart utilization.

Only about twenty percent of BD donors in Japan have been fitted in a so-called standard criteria donor for heart. Therefore, it is very important for us to maximize the number of transplantable hearts in order to

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resolve the severe donor shortage in Japan. [2] From these aspects, the purposes of donor management are not only to stabilize donor's hemodynamics until heart procurement surgery but also to maximize donor heart availability and to improve function of extended criteria donor hearts. If heart availability is increased, more patients can be saved by HTx. Maximizing donor heart availability is also the last wish of donors and donor families. However, if a heart recipient died of PGD due to a marginal donor heart, the donor family feels the loss of their lover again. Therefore, prevention of PGD is essential for the donor family as well as for recipients.

Full-scale donor management begins after the patient is sentenced BD and his or her family agrees to do so, especially in Japan. In general, donor management is based on treatment of cardiac and respiratory dysfunction resulting in improvement of hemodynamics, oxygen supply and finally other organ function as well as heart function. The targets of hemodynamic parameters are systemic blood pressure > 90 mmHg, central venous pressure (CVP) 6 to 10 mmHg, urine output 100 ml/hr (0.5 to 3 ml/kg/hr) and heart rate 80 to 120 /minutes. As organ procurement surgery begins within 12 hours after full-scale donor management is started, it is very different from usual intensive care to stabilize hemodynamics and to maintain and improve heart function in the short period. Moreover, it is important for the physicians who perform donor management to recognize the pathophysiology of BD from the beginning to completion period.

2. PATHOPHYSIOLOGY OF BRAIN DEATH

1.) Physiological Changes at Completion of Brain Death

Novitzky et al. presented a short-lived, but devastating, catecholamine (CA) "storm" by inflating a balloon in the cranial cavity in his baboon model [3,4] and showed that the hemodynamic response was a significant elevation of the systemic vascular resistance (SVR), resulting in systemic hypertension, acute left ventricular failure, fall in cardiac output, acute transient mitral valve regurgitation, leading to a rise in left atrial pressure. These events led to blood volume displacement into the venous compartment, with pulmonary edema. The electrocardiogram (ECG) showed multiple arrhythmias plus ischemic changes in all animals. However, when the intracranial pressure is increased slowly, the animals underwent a lesser hyperdynamic response, and experienced only approximately 25% of the rise in serum adrenaline (AD) levels seen in animals undergoing sudden BD. In the human clinical situation, there is a broad spectrum of adverse hemodynamic instability that is observed, which may, in part, reflect the speed at which BD is developed.

In clinical settings, BD is associated with a massive increase in CA levels sometimes resulting in increased heart rate, systemic blood pressure, cardiac output and SVR. The consequences of autonomic storm are an imbalance between myocardial oxygen demand and supply, which triggers metabolic functional alterations and sometimes heart damage (myocytolysis and necrosis). [5] Histological examination of cardiac tissue exposed to an autonomic storm shows changes typical of widespread ischemic damage and necrosis, and profound end-organ vasoconstriction has been demonstrated in animal models. [6] However, this period of intense CA release is short-lived (typically minutes) and self-limited, and may require no treatment.

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2.) Absent or Decreased Secretion of Anti-Diuretic Hormone (ADH) After Brain Death

The anti-diuretic hormone (ADH) is formed in the supra-optic and paraventricular nuclei of the hypothalamus by cleavages of a preprohormone of 168 amino acids and then a prohormone; ADH is transported to the posterior lobe of the pituitary gland which stores it. The effects of ADH result from stimulation of V1 and V2 receptors, V1 mainly responsible for vasoconstriction, V2 for the antidiuretic effect.

The effects of BD on the hypothalamic-hypophyseal axis are profound. The most frequent and almost immediate manifestation is diabetes insipidus due to loss of ADH secretion secondary to sepraventricular and paraventricular hypothalamic nuclei ischemia. ADH was undetectable within six hours. As ADH is secreted from peripheral tissues, undetectable levels of ADH have been noted in 75% of BD. As antidiuretic action of ADH is decreased, the kidneys are unable to concentrate urine and excrete large amounts (4 mL/kg/h) of dilute urine (specific gravity : <1.005 and urine osmolality: <200mOsm/L). Polyuria may lead to hypernatraemia (>145 mEq/mL), which is common and sometimes severe and worsening and associated with rising serum osmolality and hypovolemia. As the vasoconstrictive effect of ADH is decreased, the vascular tone of systemic arteries is decreased to lead to hypovolemic shock. Therefore, absence or decreased secretion of ADH after BD is associated with hemodynamic instability and compromised transplanted organ function.

Low-dose arginine vasopressin, in addition to treating diabetes insipidus, results in reduced inotropic requirements and has been associated with improved kidney, liver, and heart graft function. [3, 7-9] Pure vasopressors, like ADH, are less likely to cause metabolic acidosis or pulmonary hypertension and may be more appropriate than noradrenaline (NAD) for the vasoplegic shock phase.

3.) Cessation of Autonomic Nerve Regulations on Circulation

After brainstem ischemia and necrosis, the brain-heart connections are definitively disrupted. BD results in complete cessation of normal variations of the autonomic cardiovascular centers and a cessation of the baroreflex function [10]. Disrupted brain-heart connections, so called denervation are also observed in heart transplant recipients. Transplanted hearts could not augment cardiac performance rapidly in response to acute decrease in the preload due to loss of the brain-heart connection [11]. In normal hearts, if a preload of the heart rapidly decreases, autonomic sympathetic nerves are activated thorough vagal reflexes resulting in an increase in heart rate and cardiac contractility. However, the transplanted hearts do not increase their rate or contractility by autonomic response to a rapid decrease in preload. The augmentation of cardiac performance of the transplanted hearts depends mainly on an increase in AD secretion from the adrenal gland. Thus, the transplanted heart has been thought to be unable to rapidly enhance performance in response to a rapid decrease in the preload, such as sudden hemorrhage or occlusion of the inferior vena cava.

As shown in heart transplant recipients, hemodynamics of BD persons is also unstable. For example, a decrease in blood return to the heart due to hemorrhage, putting pressure of the upper abdomen or postural change may easily cause hypotension. After a few minutes of hypotension, AD is secreted from adrenal glands due to spinal reflex and hypertension usually up to 150 mmHg and tachycardia may be observed. In uncontrolled BD

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persons, systemic blood pressure and heart rate may rise and fall. This phenomenon is usually seen in a patient with hypovolemia due to diabetes insipidus. An increase in AD secretion may reduce the density of beta-adrenergic receptors (BAR) on the vessels and the myocardium.

4.) Alteration of BAR Systems

Various changes in BAR systems occur during and after BD. D'Amico et al. [12] reported a decrease in BAR density during BD in adult and pediatric pigs. Deterioration of myocardial performance after BD correlated temporally with desensitization of the myocardial BAR signal transduction pathway. Authors have previously reported that myocardial BAR may be depressed by the large doses of CAs used to maintain donor hemodynamics after BD. [13] The authors also revealed a significant inverse correlation between Bmax which meant BAR density and serum AD level, but not between Bmax and serum NAD or DA levels [14]. Bmax values in patients treated with AD were significantly lower than those in patients treated without AD; there was a significant inverse correlation between Bmax and the administered dose of AD. These data suggest that exogenous AD reduces BAR density in BD patients and support the conventional criteria in which retrieval of cardiac grafts is restricted to donors who can be managed with minimal to moderate levels of inotropic support.

3. Donor Assessment and Management System in Japan

1.) Medical Consultant System in Japan

Since BD organ Tx was started on 28th February 1999, every organ procurement team has taken their own staff physicians to the procurement hospital. They evaluated the condition of donor organs by ultrasound examinations for the heart and abdominal organs and BFS by themselves in ICU, before procurement operation. [2]

Since November of 2002, special transplant management doctors (a medical consultant; MC) who were usually cardiac Tx surgeons have been sent to the procurement hospital. They assessed donor organ function and identified which organs were useful for Tx. They also intensively manage the donor by giving ADH (a bolus infusion in a dose of 0.01 U/kg followed by a drip infusion in a dose of 0.01 U/Kg/hr), reducing the dose of intravenous inotropes as much as possible, and improving the donor organ function by preventing and treating lung infection before procurement teams arrived at the donor hospital.

Since the 50th BD donor in December 2006, management of lungs has been modified. In all donors, regular toileting and turning of the donor were done as previously. If there were symptoms and/or signs of atelectasis or pneumonia in chest x-ray and CT chest scan, repeated BFS and frequent toileting were performed. Since 2011, lung transplant surgeons played a role in the evaluation and managing of lungs.

Currently, MCs consists of about 30 cardiac Tx surgeons, about 40 lung Tx surgeons and several liver Tx surgeons.

1st Step Donor Evaluation

Procurement Tx coordinators (PTC) of Japan Organ Tx Network (JOT) were called to a donor hospital if there was a potential BD donor. They access the patient's clinical course and check clinical records in order to find out whether the patient is suitable for organ donation such as no absolute contraindications for organ donation, such as untreated malignancy and severe viral infections. They get informed consent for BD organ donation from his or her family.

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Then legal examination for BD is carried out.

2nd Step Donor Evaluation

After completion of the 1st clinical examination for determining BD, MCs were sent to the hospital. They and JOT PTC check clinical records such as clinical course before and after BD, medication given, blood examination, ECG, chest x-ray and abdominal and chest CT scan. The ultrasound examination for heart, liver, pancreas and kidneys and BFS is performed. MCs also rule out malignancies from findings of CT scan and ultrasound examination. JOT PTCs make donor evaluation sheets which is sent to Tx centers later.

After the 2nd clinical examination for determining BD is completed and the patient is declared death. Donor information such as donor evaluation sheets and images of ECG, chest x-ray, ultrasound examinations, BFS and CT scans is sent to transplant centers using a mobile system. Then transplant centers can decide whether their recipient should undergo Tx from that BD donor and their procurement team is sent to the hospital.

3rd Step Donor Evaluation

After arriving at the donor hospital, the procurement team also evaluates the condition of the donor organs by ultrasound examinations of the heart and abdominal organs and BFS by themselves in ICU, before procurement operation. [6] They will assess organ function and determined whether the organ could be transplanted to their recipient.

Final Donor Evaluation

After opening the chest and abdomen, the procurement team will evaluate organs by inspection and palpation. Liver biopsy is performed to rule out fatty liver and malignancies. They also look out for unexpected malignancies in the pleural and abdominal cavities.

2.) Assessment for Donor Heart Eligibility

The real goal of donor heart assessment is not to estimate the functional status of the heart just before the organ harvesting but rather to predict the performance of the transplanted graft after weaning it from the extracorporeal circulation and in the postoperative period. One also has to take into account the cumulative injury by “preexisting damage” of the donor heart and “BD-related stress”. This cumulative damage/stress may still be functionally inert but become evident after subsequent damage by ischemic time and reperfusion.

Hemodynamic Assessment Before and After Brain Death

For the hemodynamic assessment as well as for the appropriate management of the donor, the following information is important: cause of BD, clinical course and pathophysiology of BD, past history of heart disease, treatment of the patients, especially doses of inotropes [DOA/dobutamine (DOB).AD and NAD], ADH, other pituitary hormones, and antibiotics, fluid intake and transfusion, urine output, hemodynamic parameters, such as mean arterial pressure (MAP), preload and afterload [CVP, PCWP/LAP, pulmonary arterial pressure (PA)], cardiac output and/or mixed-venous oxygen saturation, i.e. from arterial and venous lines as well as a pulmonary artery catheter. Mainly, the hemodynamic assessment has to differentiate between the three most common cardiovascular problems after BD: 1) hypovolemia due to diabetes insipidus because of BD-related hypophyseal insufficiency 2) BD-related peripheral vasoplegia and 3) myocardial

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insufficiency as a result of combined pre-existing and BD-induced damage.

As shown by an analysis in 1719 consecutive primary heart Txs performed at 27 institutions, donor hearts requiring inotropic support of up to 6μg/kg/min of DOB or DOA can be accepted as so-called "marginal grafts" with acceptable outcome. [15]

Even if the donor has a history of cardiopulmonary resuscitation longer than 5 minutes, the heart might be eligible for Tx, if hemodynamics, cardiac function, wall motion of left ventricle and ischemic changes in ECG are restored under optimal donor management. [16, 17]

Chest X-Ray

Cardiomegaly, chest trauma or pleural effusions are checked by chest x-ray.

Electrocardiogram (ECG)

Most BD donors have some degree of myocardial insufficiency caused by combined pre-existing and BD-induced damage, ECG usually shows abnormality in ST segments and QRS wave. Subendo-cardial ischemia and necrosis occur accompanied by ST-elevation, Q-waves, multifocal ventricular ectopic beats and runs of ventricular tachycardia in ECG as well as transient ischemic mitral valve incompetence with an increase of left atrial pressure (LAP). These circumstances are regarded as responsible for the reversible wall motion abnormalities mentioned above.

Sustained abnormalities in ST segments and QRS and multifocal ventricular ectopic beats under optimal donor management are considerably high risks for heart Tx.

Echocardiography

Echocardiography allows a reliable assessment of cardiac valve function and myocardial hypertrophy as well as evaluation of congenital malformations. However, the assessment of myocardial performance is problematic since global and even regional ventricular dysfunction may be BD-induced and these wall motion abnormalities may be reversible within hours after optimized donor management and recovery these marginal organs can be transplanted with excellent results. Therefore, serial echocardiography is required before a graft is rejected because of myocardial dysfunction.

In the presence of LV unveiling, LV seems to be hypertrophic or to have suitable LV systolic function. Therefore, circulatory blood should be estimated by CVP, PCWP or the size and respiratory movement of the inferior vena cava (IVC) as well as the doses of inotrope prior to undergoing echocardiography to assess cardiac function.

Coronary Angiography

In the western countries, asymptomatic coronary atherosclerosis is common even in children and young people. The prevalence of significant coronary atherosclerosis – defined as a 50% stenosis of at least one main coronary artery – is found in about 20% (including 3% coronary occlusions) in a "healthy" population with a mean age of 20 to 25 years. Therefore, coronary angiography, at least in donors older than 40 years or according to the anamnesis and/or risk factors – is a "sine qua non" for the adequate evaluation. However, up until now there is no evidence which kind or degree of transmitted coronary atherosclerosis really impairs the post-transplant outcome since angiography in donors younger than 60 years has been regarded as unnecessary. On the other hand, although there are individual patients with excellent long-term outcome despite significant and (postoperatively) well documented transmitted coronary atherosclerosis, probably many of those Txs

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end in so-called "early graft failure". Recent infarction and diffuse coronary sclerosis are contraindications without any doubt, but a single stenosis with good performance of the dependent myocardial area seems to be acceptable, especially if it is treated interventionally during donor angiography or by concomitant bypass surgery during Tx. [18]

In the future, contrast computed tomography (CT) scan, especially cardiac CT scan might be useful to rule out coronary artery disease in the donor heart.

3.) Donor Management to Stabilize Hemodynamics and Maximize Donor Organ Availability

In order to manage a donor properly, hemodynamics, respiratory function, infection and other organ functions of the donor should be undertaken precisely. As there are no specific strategies for liver or renal dysfunction, cardiopulmonary management to improve organ perfusion and blood gas and metabolic management are the main therapeutic strategies for management of extended criteria donors.

Role of echocardiography and circulatory management

The aggressive assessment and optimal management of donor left ventricular (LV) dysfunction offer a tremendous potential to increase cardiac donor utilization as a significant proportion of hearts are declined for reasons of 'poor ventricular function'. However, strong evidence indicates that grafts from younger donors with left ventricular dysfunction can completely recover to normal function over time in the donor and following transplantation into a recipient [19]. Although echocardiography is very effective in screening for anatomical, especially valvular anomalies of the heart, use of a single echo examination in terms of a 'snapshot assessment' of pump function to determine the physiological suitability of a donor graft is not well supported by evidence.

Instead, better physiological assessment and donor management of LV dysfunction are achieved by Swan-Gatz catheterization (SGC) investigations, which have led to favorable long-term outcomes [20]. By serial SGC investigations, specific physiologic targets such as mean blood pressure >60 mmHg, central venous pressure <12 mmHg, pulmonary capillary wedge pressure <12 mmHg, left ventricular stroke work index >15 g m/ m^2 while on only one single inotrope can be achieved resulting in specified hemodynamic categories [20].

In the presence of LV underfilling, LV seems to be hypertrophic or to have suitable LV systolic function. Therefore, circulatory blood should be estimated by CVP, PCWP or the size and respiratory movement of inferior vena cava (IVC) as well as doses of inotropes prior to undergo echocardiography to assess cardiac function.

The goals of hemidynamic management are to achieve euvolemia, to adjust vasoconstrictors and vasodilators to maintain a normal afterload, and to optimize cardiac output without relying on high doses of beta-agonists or other inotropes, which increase myocardial oxygen demands, deplete the myocardium of high-energy phosphates, and the density of BAR in the vessels and the myocardium. Target levels of hemodynamic parameter are followed; systemic blood pressure > 90 mmHg, CVP 6-10 mmHg, urine output 100 ml/hr (or 0.5-3 ml/kg/hr) and heart rate 80-120/minutes.

Role of bronchofiberscope (BFS) and respiratory management

A ventilatory strategy with high tidal volumes is potentially harmful and may exacerbate donor lung injury already

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triggered by the systemic inflammatory response. The use of low tidal volume ventilation was shown to be beneficial in a randomized controlled study for acute lung injury and acute respiratory distress syndrome (ARDS) when compared to traditional tidal volumes. No such a trial has been performed to look if one ventilatory mode is superior to another in the care of the brain dead organ donor. However, given similarities in the pathophysiological changes occurring in ARDS and lung injury after brain death, we might expect that beneficial management strategies can be extrapolated.

Recruitment maneuvers are an important component of donor optimization, especially when the oxygenation is subnormal and pulmonary abnormalities are visible on chest x-ray. Atelectasis is a common finding in the lungs of cadaveric donors due to prolonged ventilation in the supine position. Prevention of atelectasis will reduce the development of atelectrauma by cyclic closing and reopening of collapsed lung regions. Recruitment strategies include pressure controlled ventilation with an inspiratory pressure of 25 cm H_2O (should be less than 30 cm H_2O) and a positive end-expiratory pressure of 15 cm H_2O for a short interval (2 hours) before turning to conventional volume controlled ventilation with a tidal volume of 10 mL/kg and endo-expiratory pressure (PEEP) of 5 cm H_2O. To prevent loss of alveolar recruitment, higher levels of PEEP should be used immediately after these maneuvers. Bronchoscopy should be routinely (6 to 8 hours interval) performed on all potential lung donors to assess for airway damage and visible signs of infection. Regular suctioning of retained secretions through a closed ventilator circuit may be beneficial to improve gas exchange. Target ranges of partial pressure of oxygen and carbon dioxide in arterial blood (PaO_2 and $PaCO_2$) are 70-10 mmHg and 30-35 mmHg, respectively. To protect lungs, inspired fraction in oxygen (FiO_2) should be kept as low as possible.

Postural change and air tract aspiration may cause hypotension due to a decrease in blood return to the heart in brain dead persons. From theses aspects, it is very important to stabilize hemodynamics by using ADH. If one side of the lung was not suitable to be transplanted due to pneumonia, the other side of the thorax is held up to prevent purulent sputa coming into the healthy lung.

Administration of ADH

Low-dose arginine vasopressin, in addition to treating diabetes insipidus, results in reduced inotropic requirements, and has been associated with good kidney, liver, and heart graft function as shown previously. As ADH is also effective to improve vascular tone and BAR system, ADH should be given even in patients with low urine output. ADH may improve hemodynamics and renal function resulting in an increase in urine output as shown in patients with postcardiotomy or septic shock [21].

Desmopressin is beneficial primarily for treatment of diabetes insipidus in organ donors and is not usually associated with reduction of inotrope requirements [22]. Furthermore, there is one report indicating that desmopressin may be associated with a higher incidence of human pancreatic graft thrombosis [23].

ADH should be given through CVP line with a continuous dose of 0.01-0.02 U/Kg/hr or 0.5-1 U/hr after an initial bolus dose of 0.5 to 1U [2, 24]. If hymodynamics improves, NAD, and then AD should be tapered off rapidly in favor of DOA or DOB [2, 24]. If internal and external adrenaline become in a normal range, heart rate is usually in a range of 90 to 120 /minutes. ADH should be given until cannulation of all procured organs becomes ready and heparin is given to keep

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stable hemodynamics during the procurement operation [2].

Diabetes insipidus may cause high urine output, high serum sodium, low serum potassium, high serum osmorality, reduced circulatory blood volume and reduced intracellar fluid, resulting in liver or renal dysfunction and arrhythmia. To prevent or treat these consequences, ADH administration is also important for donor management [2, 24].

Adjustments of serum sodium (135-150 mEq/l) [25] and potassium (3.8-4.5 mEq/l), hematocrit (>30%), blood sugar (120-180 mg/dl) and body temperature (35.5-36.5℃) are also important.

4.) Pre-procurement meeting and management of the procurement operation

Before starting the procurement operation, all procurement surgeons, anesthesiologists and OR nurses gathered in the meeting room. They negotiated on the types of procured organs, how to procure each organ (e.g. organ dissection/perfusion technique, incision lines, blood drainage technique, et al), what kinds of samples (e.g. blood, lymphnodes and spleen) were needed, and how to manage the donor during operation.

As most Japanese anesthesiologists never have an experience in the management of a procurement operation from brain dead donors, MC also supported them to stabilize the donor hemodynamics during operation. Skillful staff surgeons, not resident surgeons, harvested their donor organ.

As an inverse relationship between volume of intraoperative colloid and early lung allograft function was reported, packed red blood cells and albumin was transfused to maintain circulating blood volume and to replace proteins and fluids during procurement operation. To improve organ perfusion with preservation solution, any catecholamine was not additionally administered as possible to dilate the vessels of organs and ADH infusion and all catecholamine infusion were discontinued at the time of bolus infusion of heparin sulfate (400 U/Kg).

4. DISCUSSION

For many years, organ Txs has represented an established procedure in end-stage organ failure patients using the so-called ‘Traditional Criteria’ for an appropriate transplant donor. However, over the past two decades, there has been a considerable increase in the numbers of patients annually listed for organ Tx, and strict adherence to those ‘standard donor criteria’ resulted in a progredient undersupply of available organs with the result of significantly extended waiting times and increased mortality on the waiting list.

As a consequence of this severe shortage of donor organs, marginal donor organs have been utilized as many as possible in many countries. However, only 3207 hearts of 9971 deceased donors 32.2 (%) were transplanted in USA in 2010. As only 384 brain-dead donors have been procured in Japan for more than 17 years until the end of June 2016 because of the very strict Japanese Organ Transplantation Act, only 123 HTx would have been transplanted, if the cardiac donation rate from the deceased donors in Japan was same as in USA. These great pressures of organ shortage had made transplant programs consider the use of donor organs that would be considered marginal.

Therefore, original and sophisticated donor evaluation and management system has been established in Japan, such as MC and pre-procurement meeting and so on.

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To elucidate the role of this donor evaluation and management system, consecutive 384 brain dead heart donors since the Act was issued until the end of June 2016 in Japan, were reviewed. 284 hearts (74%) were transplanted and organ transplanted per a donor was 5.6. Donor age was <10 years in 4, 10-19 years in 12, 20-29 years in 39, 30-39 years in 53, 40-49 years in 76, 50-59 years in 64 and >60 years in 20 (unknown in 16). Cause of death of heart donors was subarachnoid hemorrhage in 95, head trauma in 53, anoxia in 58, post-resuscitation in 19, cerebral hemorrhage in 29 and others in 30.

Overall survival rates of cardiac recipients at 1 year, 5, and 10 years were 92.7, 89.6, and 81.8%, respectively (Figure 1). Patient survival at 10 years with donor aged 10-19 years, 20-29 years, 30-39 years, 40-49 years, 50-59 years and >60 years were 100, 97.4, 91.1, 87.3, 88.0 and 80.5%, respectively (Figure 2). Patient survival at 5 and 10 years from a donor with subarachnoid hemorrhage, head trauma, anoxia, post-resuscitation, and cerebral hemorrhage were 92,5 and 89.5%, 95.8 and 89.0, 90.0 and 90.0, 94.7 and 94.7, and 90.0%, respectively (Figure 3). These values were not significantly different.

Figure 1

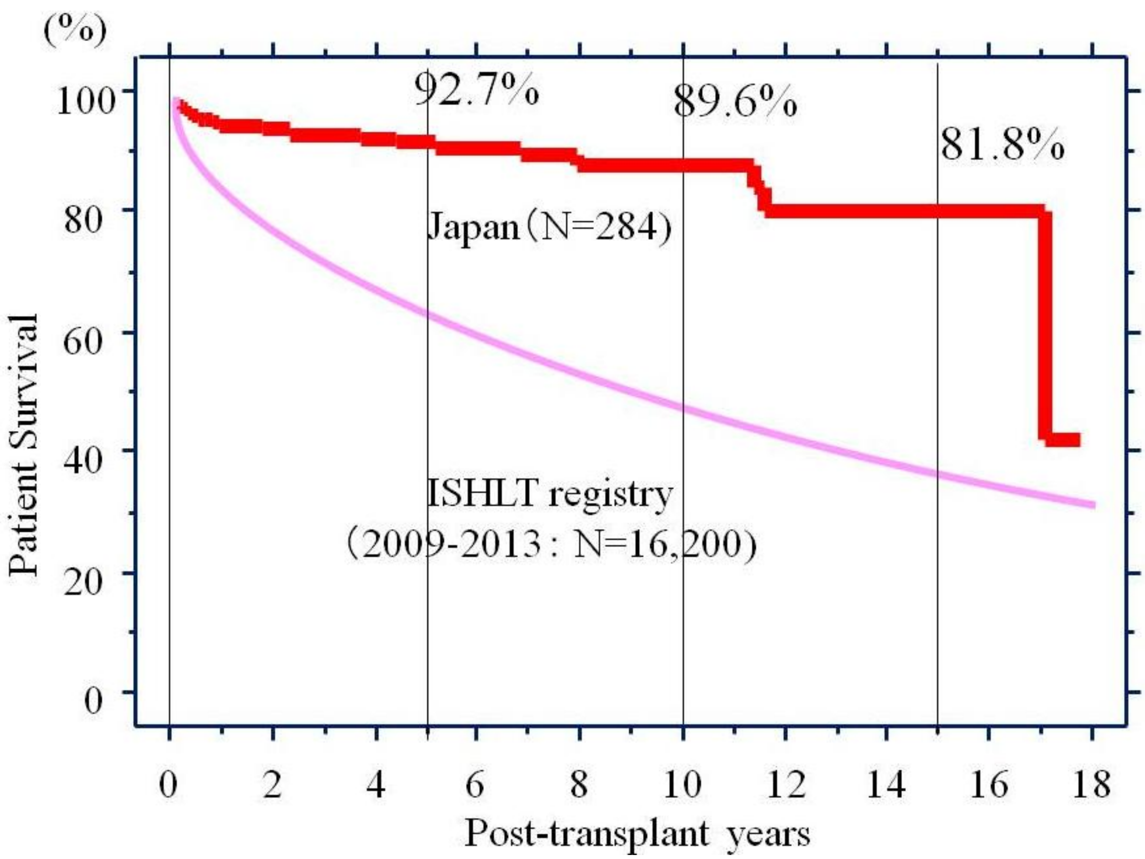

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Figure 2

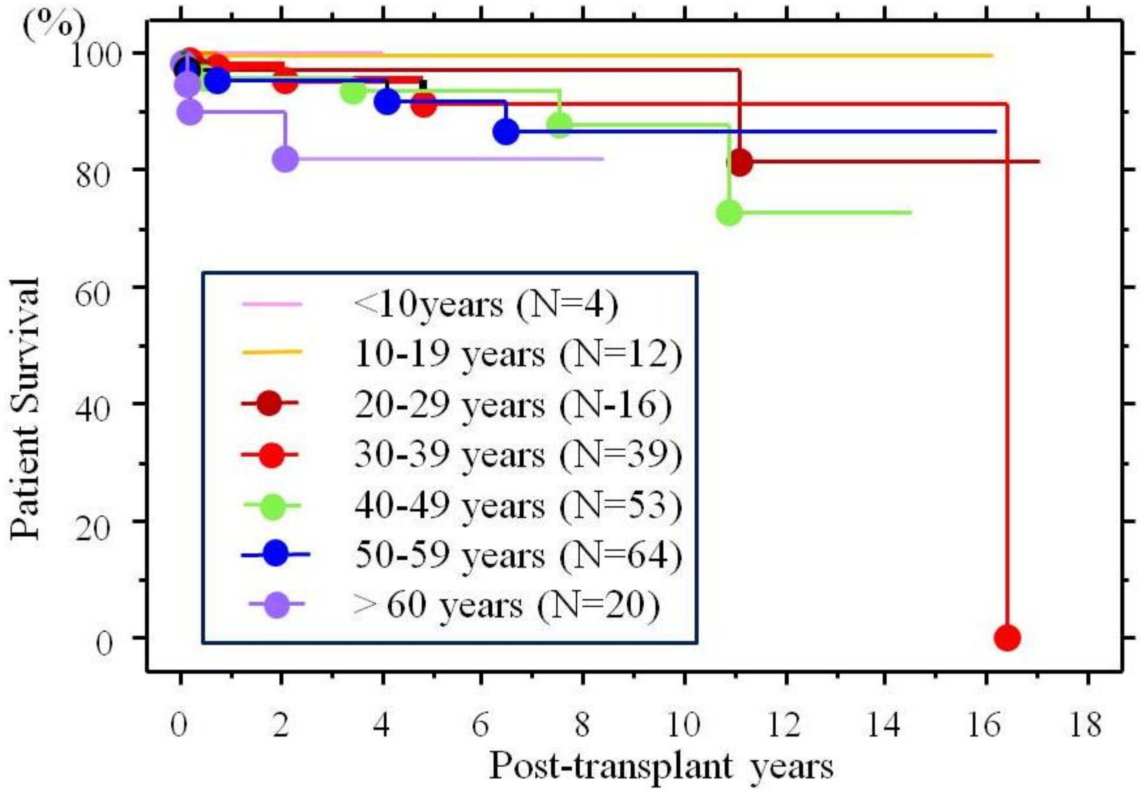
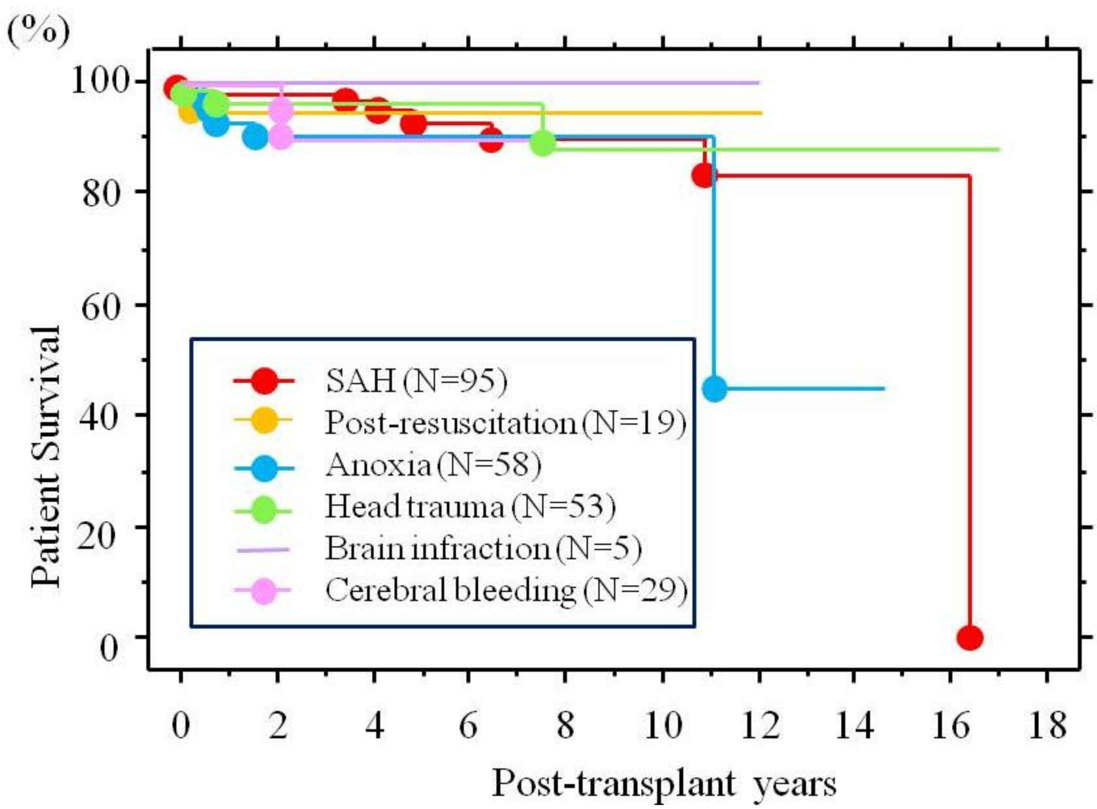


Figure 3



In conclusion, the availability of hearts has been very high and the outcomes of HTx were acceptable and medical consultant doctors may play a great role in increasing donor organ availability including a heart and in improving outcomes of cardiac recipients even from old donors or donors who died of post-resuscitation and anoxia in Japan. These strategies may be useful to maximizing heart transplant opportunities and improving post-transplant outcomes.

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