Chinese Pediatric Organ Donation With Scheduled Cardiac Arrest After Brain Death: A Novel China Classification Beyond Maastricht

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ABSTRACT

Objective. Organ donation with scheduled cardiac arrest after brain death (s-DBCD) is a special category in China. This study was to evaluate the procedure of pediatric s-DBCD, graft quality, and clinical outcomes of single kidney transplantation.

Methods. We retrospectively analyzed the data of 8 Chinese pediatric donors.

Results. The death causes of the donors (age 4–12 years) were cerebral hypoxia after cardiopulmonary resuscitation (n = 1), intracranial vascular malformation (n = 1), severe traumatic brain injury (n = 3), and brain malignancy (n = 3). The functional warm ischemia time of the grafts was 18 (13–26) minutes. Sixteen kidneys were recovered using liver-kidney en bloc procurement after in situ perfusion. All kidneys had a length >7 cm and were transplanted to 3 adolescent and 13 adult recipients. Two cases of delayed graft function occurred. The patients had a median serum creatinine level of 97 (55–123) μmol/L by the last visit. The median estimated glomerular filtration rate level was 85.4 (58–136) mL/min. Five episodes of biopsy-proven acute rejection occurred in 4 patients, which were reversed by methylprednisolone pulse therapy. Renal arterial stenosis was observed in 1 patient, which was cured by interventional balloon dilatation and stent implantation.

Conclusion. Pediatric s-DBCD is feasible with acceptable graft quality. Single kidney transplantation with pediatric graft size >7 cm has good clinical outcomes.

SINCE 2009, the Chinese government has been actively promoting legal organ donation as an important measure to relieve organ shortage. However, owing to lack of brain death legislation, organ donation after brain death is legally not feasible in China. The Health Ministry of China has made an important amendment to the donation policy by allowing a scheduled cardiac arrest for brain dead (s-DBCD) patients to facilitate lawful organ recovery [1]. The current dilemma is partly derived from an immature perception of brain death by the general public in China and the fact that laws for authentic brain death donation have not yet been put in place [2,3]. s-DBCD actually accounts for the majority of the newly increased graft pool.

Since 2010, good clinical outcomes have been reported from adult s-DBCD in China [4,5]. However, little literature focuses on pediatric s-DBCD, which has special features. For instance, there are increased risks for recovering grafts with poor quality [6]. In the current study, we retrospectively analyzed the data from 8 Chinese pediatric cases of s-DBCD and kidney transplantation outcomes at our center.

MATERIALS AND METHODS

China Classification for Organ Donation

China Category I: organ donation consistent with international standards for brain death donation (DBD) [7]; China Category II: organ donation consistent with international standards for cardiac death donation (DCD), including Maastricht Category M-I ~ V [8]; China Category III: s-DBCD–a transitional organ donation

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standard. In this protocol, brain death donors are processed with planned withdrawal of mechanical support and subsequent execution of cardiac death protocols. Category III is similar to but different from Maastricht Category IV (M-IV, refers to unplanned, nonpredictable cardiac arrest after brain death).

Organ Recovering Procedure

In the presence of donation supervisors from local authorities (Fujian Provincial Branch, China Red Cross Society), physicians from the Department of Neurology, Department of Neurosurgery, or the Intensive Care Unit diagnosed brain death for a second time. The criteria included the Diagnostic Criteria for Brain Death, the Technical Specification for Brain Death, and atropine test results. Written consents were given by the pediatric donors' parents. Then the donation procedure was initiated according to the China Guidelines for DCD [3].

With approval by the Human Organ Transplantation and Ethic Committee of our hospital (IRB00006161 – Fuzhou General Hospital IRB #1, approval number: 2010DCD; these samples were not procured from any tissue bank or other donation centers), the patients were transferred to our hospital with vital sign maintenance, which included warming, mechanical ventilating, nutritional supplement, fluid and electrolyte balancing, and blood pressure maintenance.

After arrival in the operation room, the patients were monitored with invasive blood pressure sensors. After condolence, ICU physicians withdrew mechanical ventilation and vasopressors. Five minutes after cardiac arrest, death was declared and organ recovery was initiated. The abdominal aorta and mesenteric vein were both catheterized. Liver and kidneys were jointly procured. Hypertonic citrate adenine (HCA) solution (Shanghai Blood Center, China) and University of Wisconsin (UW) solution (Du Pont, Wilmington, Del., United States) were sequentially used for perfusion, and the inferior vena cava was also catheterized for drainage. The time between systolic pressure <60 mm Hg after ventilator withdrawal and abdominal aorta perfusion was recorded as functional warm ischemia time. The actual warm ischemia time was recorded as the duration from cardiac arrest to abdominal aorta perfusion, and the cold ischemia time was recorded as the duration from perfusion to blood reperfusion during transplantation surgery. After recovery, the mortal remains were ethically handled. Renal grafts were separately prepared and the right renal veins were extended. All cases underwent right renal biopsy except for the first one (omitted).

Clinical Transplantation Procedure and Immunosuppressive Regimen

Recipient selection criteria included age (priority was assigned to children), body weight, and human leukocyte antigen (HLA) matching. Recipients were aware of and accepted the risks of receiving organs from donors with brain malignancy. The grafts were implanted into the iliac fossa, end-to-end anastomosis was used for the renal artery and the internal iliac artery, end-to-side anastomosis was used for the renal vein and the external iliac vein, and submucosal tunnel anastomosis was used for the ureter and the bladder. A 5 French double-J stent was placed, which was removed at 1 month post-transplantation.

All recipients received induction therapy with basiliximab (20 mg for adults, 12 mg/m^2 for adolescents, one dose pre-transplantation and one at day 4, Novartis, Basel, Switzerland). Intravenous methylprednisolone (8 mg/kg, Pfizer, New York, N.Y., United States) was administered intraoperatively, at day 1 and day 2 after surgery. Mycophenolate mofetil (20 mg/kg, Roche, Basel, Switzerland) and tacrolimus (0.1–0.12 mg/kg, Astellas, Tokyo, Japan) were initiated at day 1 and day 2 after surgery, respectively. Immunosuppressive drug levels were periodically determined and regimens were tailored. Anticoagulant aspirin (100 mg, Bayer, Leverkusen, Germany) was used for 1 year post-transplantation.

Follow-up Protocol

All recipients were followed up. Routine visit tests included urinalysis, complete blood count, biochemistries, and drug levels. Ordered tests included blood cytomegalovirus DNA, renal graft ultrasonography, and chest computed tomography. Pediatric glomerular filtration rate (GFR) was calculated with Schwartz formula and adult GFR with the CG formula.

RESULTS

General Data of the Donors

Seven pediatric donors were male and 1 was female (Table 1). They were negative for hepatitis B virus, hepatitis C virus, syphilis, and human immunodeficiency virus. One donor had hypoxic brain injury after cardiopulmonary resuscitation, 3 had severe traumatic brain injury, 1 had intracranial vascular malformations, and 3 had brain malignancy (medulloblastoma and rhabdoid tumor). Mild lung infection was observed before donation and antibiotics were administered. Body temperature was <38.5°C and the blood cultures were negative.

General Data of the Grafts

Sixteen renal grafts were recovered by liver-kidney joint procurement after in situ perfusion. HCA solution (1500 mL) and UW solution (800 mL) were perfused via the

Table 1. Demographic Data of 8 Pediatric Cases of Organ Donation With Scheduled Cardiac Arrest After Brain Death

Case	Sex (M/F)	Age (y)	Body Weight (kg)	Glasgow Score	ICU Duration (d)	Serum Creatinine Predonation (μmol/L)	Urine Output Predonation (mL/h)	Lung Infection	Vasopressors
1	M	4	23	3	5	56	150	Yes	Dopamine
2	M	9	32	3	8	62	100	No	No
3	M	5	24	3	5	62	100	No	No
4	M	9	36	3	26	37	100	Yes	Dopamine
5	M	11	40	3	3	87	150	No	Dopamine
6	M	7	28	3	7	72	110	No	Dopamine
7	M	8	29	3	2	59	90	No	Dopamine
8	F	12	41	3	2	81	105	No	Dopamine
Median (range)		8.5 (4–12)	30.5 (23–41)	3 (3–3)	5 (2–26)	62 (37–87)	102.5 (90–150)	No	Dopamine