Kidney Transplantation From Brain-Dead Donors: Initial Experience in China

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ABSTRACT

Background. Experience with kidney transplantation from brain-dead donors remains limited in China. Our objective was to evaluate the outcomes of kidney transplantation from brain-dead donors (group 1), compared with those from living ones of the same age (group 2).

Methods. Clinical data of kidney transplantation from brain-dead donors and living donors in the same age range (18–45 years) performed between May 2007 and December 2011 were analyzed retrospectively. Recipients were analyzed for posttransplantation serum creatinine, creatinine clearance (calculated by the Cockcroft-Gault formula), the number of acute rejection episodes and delayed graft function, and patient/graft survival.

Results. Mean donor age was comparable between the 2 groups (31.9 ± 6.5 vs 32.8 ± 7.0 years; $P = .268$). The terminal serum creatinine level of donors was 125.5 ± 63.5 μmol/L in group 1 (n = 30) and 65.1 ± 13.7 μmol/L in group 2 (n = 110; $P = .000$). Recipient creatinine clearance was comparable between the 2 groups 1 month posttransplantation and thereafter. Acute rejection episodes were seen in 7 cases in recipients of group 1 (15.9%) and in 15 cases in recipients of group 2 (13.6%; $P = .716$). The incidence of delayed graft function was higher in recipients of group 1 (18.2%) than that of group 2 (3.6%; $P = .002$). The 1-, 3-, and 5-year patient/graft survival rate was comparable between the 2 groups.

Conclusions. Our study demonstrated kidney transplantation from brain-dead donors achieved acceptable graft function and patient/graft survival in the 5-year follow-up, encouraging the use of this approach.

FOR most patients with end-stage renal disease, kidney transplantation has the greatest potential for restoring a healthy, productive life, and is generally acknowledged as the optimal therapeutic option [1]. As the number of individuals with end-stage renal disease grows, the discrepancy between available donor organs and patients waiting for transplantation widens. In China, the reduction and termination in organ supply from the prison system has resulted in the development and implementation of the modern organ donation system. Kidneys from donation after citizen death, including donation after brain death (DBD) and donation after cardiac death, has gradually replaced traditional cadaveric organs for the past several years. Experience with kidney transplantation from DBD remains limited because there is not much more than 10 years of clinical practice.

Donor brain death is considered as a risk factor of delayed graft function (DGF) and inferior long-term graft survival [2]. However, when analyzing the impact of brain death on graft outcomes, several other confounding variables should be taken into account after adjusting for recipient factors. It is acknowledged that donor age has a significant effect on kidney transplant survival [3]. In this

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retrospective study, after being adjusted with donor age, the outcomes of kidney transplantation from DBD were evaluated, compared with those from living donation (LD).

PATIENTS AND METHODS

Study Subject

Between May 2007 and December 2011, 44 DBD kidney transplants were performed in the institution of the corresponding author. The control group was composed of patients who received renal transplants from living donors in the same age range. Excluded from the study were patients who were <18 years or who underwent repeat transplantation. This study was approved by the institutional review board, and was in accordance with the 1975 Helsinki Declaration, as revised in 2000. Written informed consent was obtained from all patients.

Preoperative Evaluation of Donors

The evaluation of potential brain-dead donor was performed by the organ procurement organization according to related criteria and regulations. Brain death of donors was identified according to the following judging criteria with a second examination after an interval of 12 hours: (1) Prerequisites: (a) the cause of coma is clear and plausible, (b) Causes of reversible coma is excluded; (2) Clinical determination: (a) deep coma, (b) complete absence of brain stem reflexes, (c) lack of spontaneous respiration on disconnecting the respirator and confirmed by the apnea test; (3) Confirmation tests: (a) electroencephalogram electrical silence, (b) transcranial Doppler shows complete absence of intracranial blood flow, and (c) somatosensory evoked potential.

The determination and declaration of brain death was made by 2 medical practitioners with ≥5 years' experience of clinical practice. Organ procurement organization members and transplantation-associated practitioners were required to withdraw from the procedure.

All potential living donors underwent a thorough history inquiry and a rigorous examination. Preoperative evaluation included hematological and biochemical screening, urine microscopy, chest radiography, electrocardiogram, renal sonogram, HLA typing and matching, ^{99m}Tc DTPA renal scan, and computed tomography angiography with 3-dimensional reconstruction of the renal hilum. Potential living donors with diabetes, proteinuria, or severe heart or liver diseases were excluded. Mild hypertension was not regarded as an exclusion criterion.

Operative Procedures and Immunosuppressive Regimens

Renal grafts from DBD were procured by the organ procurement organization. A cruciate midline incision was used. The right colon and duodenum were mobilized, exposing the great vessels. The aortic bifurcation was isolated. The interior mesenteric artery and vein were ligated. Cannulas were placed for in situ flushing and cooling. The ureters were divided deep in the pelvis. The kidneys were removed en bloc with the aorta and vena cava. If multiple organs were to be removed, kidneys were removed last. Then the kidneys were separated in slush. All living donors underwent open nephrectomy through a retroperitoneal flank incision, and the left kidney was the first choice unless there were multiple arteries.

Kidneys were placed in cold hypertonic citrate adenine solution, which was jointly developed by Shanghai Changzheng Hospital and Shanghai blood center, in sterile containers for preservation and transport.

Transplant procedures were performed using the usual technique in the right or left iliac fossa with vascular anastomoses to the external iliac artery and vein. Ureteroneocystostomy was performed using the extravesical technique with a double-J ureteral catheter.

Immunosuppression consisted of induction therapy with methylprednisolone (500 mg/d for 3 days) and basiliximab (20 mg pretransplant and posttransplant day 4)/thymoglobulin (50 mg/d for 3 days), and sequential triple maintenance therapy. All patients were treated with cyclosporine- or tacrolimus-based immunosuppression (trough concentrations 150–200 6–10 ng/mL, respectively), including mycophenolate mofetil (2 g/d)/mycophenolate sodium (1.44 g/d) and prednisone (30 mg/d). The dosage of immunosuppression tapered over time. Acute rejection (AR) episodes were initially treated using methylprednisolone pulsed therapy (500 mg × 3 d). Thymoglobulin was administered in instances of corticosteroid-resistant rejection.

Follow-up of Recipients

Recipient serum creatinine (SCr) at 1 day, 7 days, 1 month, 3 months, 6 months, 1 year, and every year thereafter after transplantation, was recorded. Corresponding glomerular filtration rate was estimated using the Cockcroft-Gault formulation. The number of AR episodes and DGF was recorded. Graft and patient survivals at 1, 3, and 5 years posttransplantation were calculated. AR was either clinically diagnosed or biopsy proven. DGF was defined as the requirement of dialysis within 1 week of transplantation.

Statistical Analysis

Statistical analysis was performed with SPSS 13.0 software (SPSS, Inc, Chicago, IL). Data were expressed as mean values ± standard deviation for continuous variables and as n (%) for categorical ones by default. Continuous variables were compared using the Student t test. Categorical variables were compared using the χ^2 test. Patient and graft survival were assessed with Kaplan-Meier curves and compared with the log-rank test. $P < .05$ was considered significant.

RESULTS

Baseline Characteristics

Table 1 shows demographic and clinical date of donors and recipients. Mean donor age was 31.9 ± 6.5 in group 1 and 32.8 ± 7.0 in group 2 ($P = .268$). There were more women among the living donors. The terminal SCr level was significantly higher in brain-dead donors. There were no differences between the groups according to donor age and body weight. Recipients of DBD were older. There were no differences between the groups according to recipient gender, body weight, SCr, and time on dialysis. The median follow-up was 32 months (range, 12–67) and 49 months (range, 12–67), respectively.

Graft Function

Table 2 shows mean SCr level of the 2 groups during the follow-up period. It was higher in recipients of DBD in the initial month posttransplantation; however, the difference was no longer significant at all the time points we selected throughout the remaining 5-year study period. The estimated glomerular filtration rate was consistently comparable between the 2 groups at 1 month posttransplantation and thereafter (Fig 1).