Updates in Heart Transplantation

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ABSTRACT
Heart transplantation (HTx) has been a successful therapy for patients with end-stage heart failure. Since 1987, we have performed 288 HTx. Thirty-six subjects needed mechanical support prior to HTx. We use anti-thymocyte globulin (ATG) as induction therapy and low-dose immunosuppressive agents for maintenance treatment. In June 1996, we performed combined heart and kidney transplantation after bridging for 14 days with an indigenous total artificial heart (TAH). The patient is still well. Our actuarial survival rates at 1, 5, and 10 years are 86%, 76%, and 61%, respectively. One recipient who voluntarily discontinued all treatment at 4 years after HTx is still alive and free of rejection in his ninth posttransplantation year. The longest surviving recipient is in her 18th posttransplantation year. We also have used many suboptimal donor hearts, most with satisfactory outcomes. A 14-year-old boy had full recovery of heart function after receiving a donor heart after 13 hours of ischemia in 2003. Standard biatrial anastomotic technique is still our first choice. The incidence of tricuspid regurgitation (TR) and conduction disturbances is not higher than the bicaval technique reported by others. With low-dose therapy, our short-term and long-term results of HTx are satisfactory. The use of suboptimal donor hearts may expand the donor pool and save more patients’ lives. A biatrial anastomosis remains our surgical technique.

AFTER the first successful heart transplantation (HTx) performed by Barnard in 1966, clinical HTx was then started in other cardiac surgical centers around the world. In the early years, however, few patients were more than short-term survivors. With the introduction of newer immunosuppressive agents and improved surgical techniques, most patients may have satisfactory long-term results in the recent years. At the same time, good surgical results lead to increased demand. Using suboptimal donor hearts has become an efficient way to expand the donor pool.

MATERIALS AND METHODS
From July 1988 to November 2007, we performed 288 heart orthotopic HTx in 220 males and 68 females. The mean age was 47.4 ± 14.7 years (range, 2.7–74.9). Fifteen were pediatric cases. There were 4 combined heart-kidney transplantations. The surgical indications were dilated cardiomyopathy (CMP) in 199 (69.1%), ischemic CMP in 56 (19.4%), and other causes in 33 (11.5%).

Mechanical Support
Some patients needed mechanical support prior to HTx: intra-aortic balloon pump (IABP) in 26, extracorporeal membrane oxygenation (ECMO) in 8, left ventricular assist system (VAS) in 1, and total artificial heart (TAH) in 1. The 1 patient who received TAH was a 56-year-old man who developed profound shock after an extensive myocardial infarction (MI). He was on IABP and ECMO for 1 week, but his systolic blood pressure (BP) was still around 70 mm Hg. In June 1996, he underwent combined heart and kidney transplantation after bridging for 14 days with our indigenous TAH (Phoenix-7 model, designed by Kevin Cheng, Taiwan Artificial Heart Research Center).

Immunosuppression
We used anti-thymocyte globulin (ATG) as the induction therapy for the first 3–7 days after HTx. Other drugs included: calcineurin inhibitor (CsA in 248 and Tacrolimus in 40), antimetabolites (Azathioprine in 37, MMF in 246, and mycophenolic acid in 15), and anti-CD 25 Ab (Daclizumab in 16 and Basiliximab in 6). In the early postoperative period, we used half of the standard doses of ATG, calcineurin inhibitor, MMF, and steroids. After the first month, we gradually reduced the doses of CsA and Tacrolimus to trough blood levels of 150 ng/mL and 6 ng/mL, respectively. One hundred seventy-four cases were steroid-free after the first year.

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For highly sensitized patients (PRA >15% and retransplant recipients), we used plasmapheresis or IVIG to prevent Ab-mediated rejection (AMR).

Endomyocardial Biopsy

Endomyocardial biopsy (EMB) was performed more frequently in our early cases. Now we are doing EMB less often. The frequency is dependent on the severity of rejection in each individual.

Posttransplantation Coronary Artery Disease

Before the introduction of multi-slice computerized tomography (MSCT), the recipients received annual coronary angiogram (CAG). Now we perform MSCT instead. To study the incidence of posttransplantation CAD, we performed CAG for 192 patients who underwent HTx between 1988 and 2004.

Suboptimal Donors

Twelve donors had CPR before organ harvesting. There was also a size mismatch (BW difference ≥20%) in 81 cases. Seven patients received donor hearts from extremely under-sized donors (BW 50%–60% of recipient). The 3 pediatric patients all survived despite donor hearts from extremely over-sized donors (BW 190%–250% of recipient). We used crystalloid cardioplegia solution for preservation of the donor hearts. The longest ischemic time was 13 hours. Twenty donors were older than 50 years. For those who could not receive CAG at the donor hospitals, we performed a diagnostic CAG for the isolated heart at the recipient hospital. Contrast medium was directly injected into the coronary orifices (bench CAG). Two patients received concomitant coronary artery bypass grafting during HTx.

Surgical Technique

We used a biatrial anastomosis. We did a survey on the occurrence of tricuspid regurgitation and conduction disturbances among 244 patients who underwent HTx between 1988 and 2005.

RESULTS

The surgical mortality rate was 20/288 (6.9%), including acute cellular rejection (ACR) in 6 and AMR in 3. Late mortality rate was 56/288 (19.4%), including ACR in 21 and infection in 29. Four underwent retransplantations. Only the 1 patient who underwent plasmapheresis survived. The actuarial survival rates at 1, 5, 10, and 15 years were 86%, 76%, 61%, and 51%, respectively. Fifty-five patients were still alive at 10 years after HTx. The longest surviving patient is still well in her 18th posttransplantation year.

When we started to use MMF (3–4 g/d) in July 1997, 2 previously stable patients died of infections. Currently, we use MMF in half doses. A 61-year-old man voluntarily discontinued medications at 4 years after HTx, and is still well and free of allograft rejection in his ninth posttransplantation year. He had several HLA matches with his donor: A33 (19), BW4, and DR 13(6).

Ten patients developed malignant tumors: 3 hepatomas, 1 lung cancer, 1 cervical cancer, 1 bladder cancer, 1 gastric cancer, 1 colon cancer, 1 breast cancer, and 1 Kaposi’s sarcoma. There was complete remission of systemic Kaposi’s sarcoma at 3 months after 50% reduction of the CsA dose.

Six of the 7 patients who received hearts from extremely under-sized donors survived. All 3 pediatric patients who received hearts from extremely over-sized donors also survived. The patient who received a heart that sustained 13 hours of ischemia showed full recovery of heart function after HTx. The 2 patients who received concomitant CABG during HTx are still alive.

Thirty-six of 244 (14.8%) recipients developed moderate TR and 11/244 (4.5%) had severe TR. Only 2 patients needed a permanent pacemaker for complete heart blockage.

Among 192 patients who underwent HTx for 1 year before 2005, we observed abnormal CAG in 23 (12.0%); 8 underwent stenting, 4 CABG, and 3 retransplantation. All CABG patients survived. All retransplantation patients died. Most of the others (13/16; 81%) are still alive.

DISCUSSION

With the increased popularity of the use of mechanical support to patients awaiting HTx, many are critical before HTx due to respiratory failure, renal failure, hepatic failure, or even infection. We use low doses of medications to prevent ACR, AMR, however, remains a challenge in highly sensitized patients. Without plasmapheresis, most died of AMR. In contrast, immune tolerance may develop after HTx, such as the case without medication.

With the advance HTx, the number of candidates far exceeds the available donors. Donor criteria have been modified to accept organ donations with suboptimal conditions. (1) Donors with CAD: for hearts from aged donors or donors who died of cerebral hemorrhage, CAD may be diagnosed using bench CAG. Concomitant CABG may be performed with similar results. (2) Size mismatch: the criterion of size mismatch may be modified too. According to our experience, even 50%–60% under-sized donors may be used for adult recipients and 190%–250% over-sized donors may be used for pediatric recipients. (3) Heart ischemic time: we experienced successful use of a heart with 13 hours of ischemia.

We use a biatrial technique for every case. In our series, the incidence of TR and conduction disorders was not higher than that reported by others using a bicaval anastomosis.2 Severe TR may affect the long-term outcome of HTx patients. The literature has reported 6%–32% of recipients develop significant TR after HTx, chiefly due to chordal rupture induced by EMB.3 The McGill group reported that 60% of recipients may have TR after 31 or more EMBs.3 Our previous study also demonstrated a positive correlation between the time of onset of TR and the number of EMBs.4 We suggest not performing many EMBs after HTx.

The incidence of posttransplantation CAD among our recipients was only 12%. It might be an underestimate because the diagnosis is made using CAG instead of intra-vascular ultrasound. The results of CABG were good.
In conclusion, with low-dose immunosuppression, our short-term and long-term results of HTx are satisfactory. The use of suboptimal donor hearts may expand the donor pool and save more patients’ lives. A biatrial anastomosis remains our surgical technique.

REFERENCES


