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Hemodynamic and Echocardiographic Evaluation of Orthotopic Heart Transplantation With the Modified Bicaval Anastomosis Technique

Soichiro Kitamura, MD; Takeshi Nakatani, MD; Tomoko Kato, MD; Masanobu Yanase, MD; Junjiro Kobayashi, MD; Hiroyuki Nakajima, MD; Toshihiro Funatsu, MD; Koichi Toda, MD; Akiko Kada, MPH*; Hitoshi Ogino, MD; Toshikatsu Yagihara, MD

Background: The purpose of this study was to evaluate the hemodynamic and echocardiographic function of hearts transplanted with the modified bicaval anastomosis technique (mBCAT).

Methods and Results: Twenty consecutive patients (14 males, 6 females, age range 14–61 [41.3±11.5 years]) were evaluated 3.4±2.2 years after heart transplantation using the mBCAT. All patients were in status I on the waiting list, and 18 (90%) had had a left ventricular assist device. The donor age was 39±12 years. Triple immunosuppressive regimen and cardiac biopsy were routinely performed. There was no hospital mortality. One death occurred 4.2 years after the operation because of bone marrow dysplasia and infection. The 8-year survival was 89% (95% confidence interval: 0.43–0.98). All the hemodynamic variables returned to the normal range. Low right atrial pressure (3.2±1.5 mmHg) and low pulmonary wedge pressure (6.7±2.1 mmHg) were associated with an excellent cardiac index (3.9±0.7 $L \cdot min^{-1} \cdot m^{-2}$). Echocardiography revealed an excellent late peak velocity (52±19 cm/s) and an E/A ratio (1.4±0.6) of tricuspid flow. The grade (0–4) of tricuspid regurgitation averaged 1.5±0.8.

Conclusions: Hemodynamic and echocardiographic results for mBCAT were excellent. The 8-year survival was 89% with all surviving patients in New York Heart Association class I. The mBCAT is easy to perform and further facilitates cardiac transplantation. (*Circ J* 2009; **73:** 1235 – 1239)

Key Words: Cardiac function; Cardiomyopathy; Hemodynamics; Transplantation

The new Japanese legislation for organ transplantation from brain death donors was established in October 1996, and 49 heart transplants have been performed in Japan to the end of 2007[1,2] At the National Cardiovascular Center, 22 patients received heart transplants during the same period. Of the first 2 patients, 1 had the standard biatrial anastomosis technique (BAAT) and the other underwent the original bicaval anastomosis technique (BCAT)[2] The following 20 consecutive patients underwent transplantation using a modified BCAT (mBCAT) developed at our center[3] At present, nearly 70% of heart transplant operations in Japan use this technique, probably because of its easy applicability and some advantages[4] We report the results of a mid-term hemodynamic and echocardiographic evaluation of 20 consecutive patients who have undergone heart transplantation using the mBCAT. We also compare our results with previously published functional results of different transplant techniques.

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*Department of Organ Transplantation, Cardiovascular Surgery, *Department of Clinical Research and Development, National Cardiovascular Center, Suita, Japan*
Mailing address: Soichiro Kitamura, MD, Department of Cardiovascular Surgery, National Cardiovascular Center, 5-7-1 Fujishirodai, Suita 565-8565, Japan. E-mail: skitamur@hsp.ncvc.go.jp

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Methods

The 20 consecutive patients comprised 14 males and 6 females, ranging in age from 14 to 61 years, with a mean of 41±11 years; the body surface area (BSA) varied from 1.35 to 1.83 m^2 (mean 1.60±0.16 m^2). The diagnosis confirmed by pathological examination of the recipients' original heart was idiopathic dilated cardiomyopathy (DCM) in 17 patients, dilated phase of hypertrophic cardiomyopathy in 1 and cardiac sarcoidosis in 2. Preoperatively, 5 patients had a pacemaker and 2 had an implantable cardiac defibrillator (ICD); 18 (90%) patients had had a left ventricular assist device (LVAD) before transplantation and the remaining 2 patients had been on multiple inotropic agents, requiring intensive care. Consequently, all 20 patients were in the status 1 category. Most LVAD implantations were preceded by insertion of an intraaortic balloon pump, and the LVAD was a Toyobo type for 16 patients and a HeartMate VX device for 2. The average waiting time for transplantation from the time of registration with the Japan Organ Transplant Network and that of heart transplantation varied from 59 to 2,748 days, with a mean of 947±697 days, and the period on LVAD was 702±366 days, varying from 99 to 1,444 days.

Pre- and postoperative cardiac dimensions were assessed by ultrasound cardiography, and hemodynamics were evaluated by cardiac catheterization using a Swan-Ganz catheter.

Table 1. Demographics of 20 Patients Who Underwent Heart Transplantation With the mBCAT

Male/female	14/6
Age (years)	41.3±11.5 (14–61)
Height (cm)	166±10 (146–175)
Weight (kg)	54.2±9.8 (41.5–77.6)
BSA (m^2)	1.60±0.16 (1.35–1.83)
BMI	19.3±2.7 (14.8–23.8)
Blood type	A 7, B 1, O 9, AB 3
Diagnosis	DCM 17, dHCM 1, cardiac sarcoidosis 2
LVAD	18 (90%)
LVAD supported time (days)	702±366 (99–1,444)
Waiting status I	20 (100%)
Waiting time (days)	947±697 (59–2,748)
Donor age (years)	39±12 (18–54)
Total ischemic time (min)	207±26 (137–255)
Rejection episode > grade 2 (times/patient)	1.1±1.4

Values are mean±SD (range).
mBCAT, modified bicaval anastomosis technique; BSA, body surface area; BMI, body mass index; DCM, dilated cardiomyopathy; dHCM, dilated phase of hypertrophic cardiomyopathy; LVAD, left ventricular assist device.

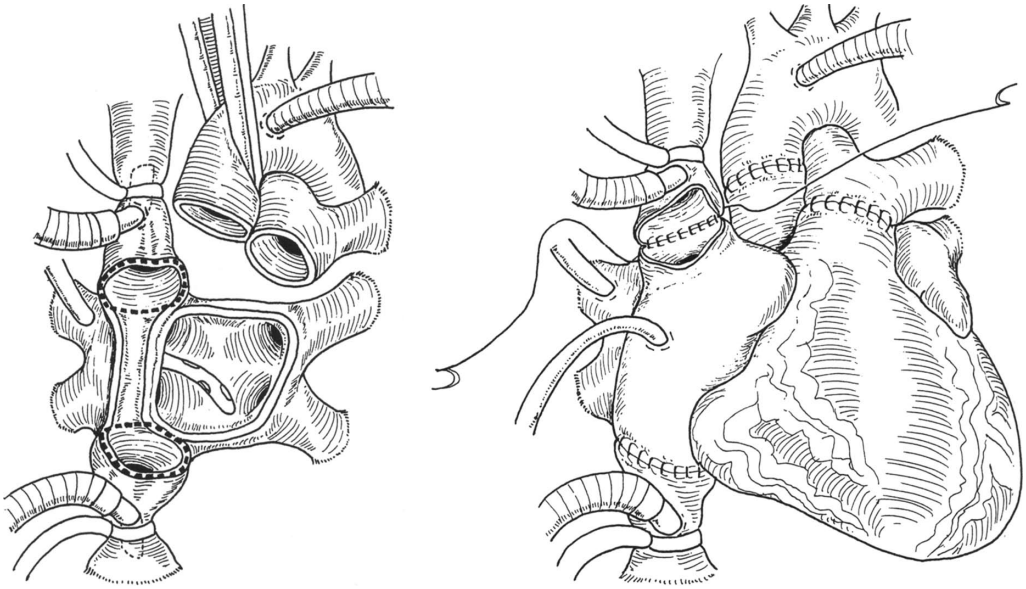

Figure 1. (**Left**) The modified bicaval anastomosis technique. The posterior right atrial wall is left undivided as a cuff bridging the superior and inferior venae cavae to maintain the anatomical orientation without traction, kinking or distortion of the superior and inferior venae cavae. (**Right**) By expanding the suture line into the preserved posterior wall of the right atrium, anastomosis with a large donor heart can be easily accomplished. Also, adjustment of the distance between the superior and inferior venae cavae can be done with ease when the donor heart is small.

Assessment of the pre-transplant hemodynamics and plasma brain natriuretic peptide (BNP) level was performed prior to LVAD installment. Post-transplant studies were done 3.4±2.2 years after operation. The demographics of the 20 patients are listed in **Table 1**.

Operation

Donor Heart Procurement The age of the donors averaged 39±12 years, ranging from 18 to 54 years. The donor hearts were recovered at various locations in Japan and usually transported by jet charter flight unless they were retrieved at a near-by hospital in which case road transport was used. For the most of recent patients (80%), Celsior solution[5] was used for both cardioplegic arrest during extraction and storage during transportation, whereas for the initial 4 patients in this series, St Thomas solution was used.[2] The total ischemic time from cardiac extraction to aortic declamping at the final stage of the transplant procedures varied from 137 to 255 min with a mean of 207±26 min.

Transplant Procedure The transplantation procedure used in the present series was the mBCAT, reported by us in 2000.[3] Briefly, the posterior right atrial (RA) wall is left undivided as a cuff connecting the superior (SVC) and inferior venae cavae (IVC), as illustrated in **Figure 1**. Without complete division and separation of the SVC and IVC their anatomical orientation is well maintained and the distance required for the graft tissue to fit exactly between them is easily judged, thereby avoiding traction, kinking or distortion of either of the vessels. This modification is particularly useful when there is a size mismatch between the donor and recipient hearts.

Postoperative Management and Episodes of Rejection Triple immunosuppressive regimen was routinely used. All patients, except 4 (80%), started with Neoral (cyclosporine

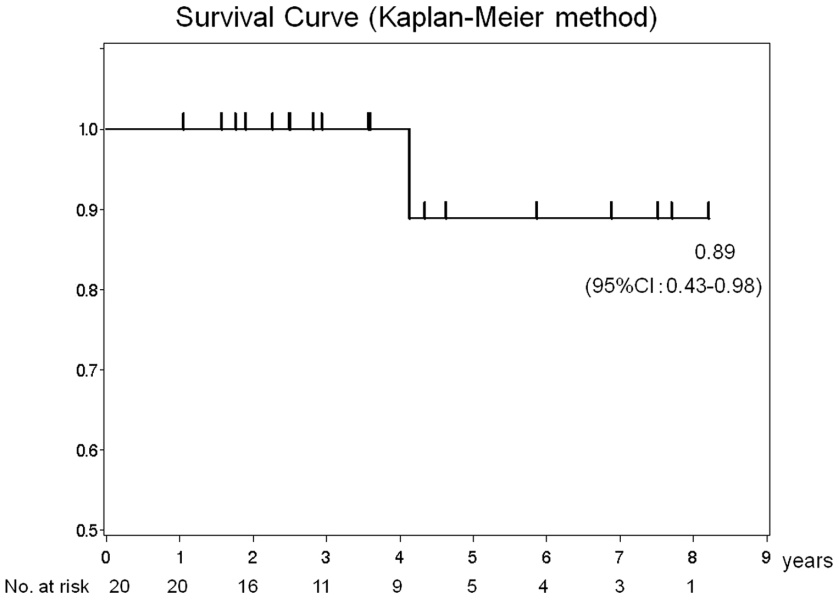

Figure 2. The 8 years survival of 20 consecutive patients with a heart transplanted using the modified bicaval anastomosis technique was 89% with a 95% confidence interval (CI) of 0.43 to 0.98. All surviving patients are in New York Heart Association class I at present.

Table 2. Pre- and Post-Transplant Hemodynamic Variables

	Pre-OP (n=20), mean±SD	Post-HTx (n=20), mean±SD	P valve
Echocardiography			
LVDd (mm)	72.0±8.5	40.7±4.9	<0.001
LVDs (mm)	65.2±9.0	24.9±4.1	<0.001
EF	0.20±0.08	0.6±0.07	<0.001
FS (%)	10±4	40±6	<0.001
IVS thickness (mm)	7.3±2.0	9.0±1.3	<0.001
PW thickness (mm)	7.3±1.9	8.9±1.3	<0.001
Catheterization			
HR (beats/min)	88±9	92±7	0.089
CO (L/min)	3.1±0.7	6.1±1.2	<0.001
CI ($L \cdot min^{-1} \cdot m^{-2}$)	1.9±0.4	3.9±0.7	<0.001
PAWP (mmHg)	25.8±0.6	6.7±2.1	<0.001
PAs (mmHg)	45.8±15.7	20.8±3.8	<0.001
PAd (mmHg)	20.6±9.0	7.8±2.2	<0.001
PAm (mmHg)	31.0±11.0	13.0±2.6	<0.001
RVs (mmHg)	45.5±16.0	23.0±4.0	<0.001
RVEDP (mmHg)	11.3±5.5	4.4±1.8	<0.001
RA (mmHg)	11.7±5.5	3.2±1.5	<0.001
TPG (mmHg)	5.3±7.0	6.3±2.7	0.56
PVR (WU)	1.7±2.3	1.1±0.6	0.25
Plasma BNP (pg/ml)	725±291	55±49	<0.001

OP, operation; HTx, heart transplant; LVDd, left ventricular diameter (diastolic); LVDs, left ventricular diameter (systolic); EF, ejection fraction; FS, fractional shortening; IVS, interventricular septum; PW, posterior wall; HR, heart rate; CO, cardiac output; CI, cardiac index; PAWP, pulmonary artery wedge pressure; PAs, pulmonary artery pressure systolic; PAd, pulmonary artery pressure diastolic; PAm, pulmonary artery pressure mean; RVs, right ventricular systolic pressure; RVEDP, right ventricular end-diastolic pressure; RA, right atrial pressure; TPG, trans-pulmonary pressure gradient; PVR (WU), pulmonary vascular resistance (Wood units); BNP, brain natriuretic peptide.

A), Cellcept (mycophenolate mofetil), and prednisone[6] Prograf (tacrolimus) was selected as the first calcineurin inhibitor in 4 patients, mainly to enhance our clinical experience with this drug. Serum concentrations of cyclosporine A, tacrolimus and mycophenolate mofetil were routinely monitored to facilitate dose adjustment[7]

Endomyocardial biopsy was performed according to schedule in the usual manner. Rejection was judged microscopically, based on the criteria of the 1990 report of the International Society of Heart and Lung Transplantation[8] with reference to the 2004 revision[9] Rejection episodes greater than grade 2 occurred 1.1±1.4 times per patient during the follow-up. Rejection of more than 3A was identified in 2.7% of 340 biopsy specimens from the 20 patients, and was successfully controlled by steroid pulse therapy, switching cyclosporine A to tacrolimus or a combination.

Statistical Analysis

Values are mean±standard deviation. Pre- and post transplant cardiac dimensions and function in each patient were compared by paired t-test. Survival was calculated by the Kaplan-Meier method. Differences were judged statistically significant at $P<0.05$.

Table 3. Post-Transplant Trans-Atrioventricular Valve Flow and Regurgitation by Echocardiography

	Tricuspid valve (n=20)	Mitral valve (n=20)
Regurgitation (grade 0–4)	1.5±0.8 (0–3*)	0.6±0.6 (0–2)
Late peak velocity of flow (cm/s)	52±19	40±11
E/A ratio	1.4±0.6	2.2±0.7

*Grade 3 tricuspid regurgitation resulted from chordal damage at endomyocardial biopsy (1 patient).

Results

Survival

There were no operative or hospital deaths and all patients were successfully discharged from hospital. A 59-year-old male patient died 4 years and 2 months after transplantation. His postoperative course was complicated by dysplasia of the bone marrow and cytomegalovirus gastric ulcer requiring an emergency gastrectomy. The final cause of death was pneumonia. The remaining 19 patients were all doing well in New York Heart Association class I, and the Kaplan-Meier survival rate up to 8 years was 89% (95% confidence interval 43–98) (**Figure 2**). No one required a pacemaker or ICD implantation after transplantation.

Hemodynamic and Echocardiographic Assessments

The hemodynamic and echocardiographic assessments of the heart before and after transplantation are shown in **Tables 2**,**3**. After transplantation, all cardiac function parameters and dimensions completely returned to normal. Preoperative and post-transplant differences in the hemodynamic and echocardiographic variables were all markedly significant at $P<0.001$, except for heart rate ($P=0.089$) and pulmonary vascular resistance ($P=0.25$). All patients were in normal sinus rhythm. The mean RA pressure in the mBCAT patients was 3.2±1.5 mmHg. There were no measurable pressure gradients between the SVC or IVC and the RA. The late peak velocity of tricuspid flow was 52±19 cm/s and the E/A ratios of tricuspid and mitral flow were 1.4±0.6 and 2.2±0.7, respectively. The incidence of moderate to severe tricuspid valve regurgitation (TVR) was 5%, with a mean grade of 1.5±0.8 (range 0–3). In 1 patient in this series, chordal injury of the tricuspid valve accidentally occurred at the time of endomyocardial biopsy, which resulted in grade 3 TVR. The pre-transplant plasma level of BNP was 725±291 pg/ml (range 342–1,099) and it was significantly reduced to 55±49 pg/ml (range 5–172), postoperatively ($P<0.0001$).

Discussion

Orthotropic heart transplantation is a well-established treatment for end-stage heart failure and the post-transplant recovery of patients is dramatic. Although life-long care for the control of rejection and infection is necessary, this has significantly improved in recent years. As shown in this study, the grade of hemodynamic improvement with heart transplantation was really excellent, with a resultant 8-year survival of 89%, in contrast to that for left ventricular restoration surgery for congestive heart failure because of DCM.[10]

On the other hand, operative techniques for heart transplantation have not changed significantly from the original BAAT developed in the experimental era by Shumway, Lower, and Stofer.[11] The only option to the standard BAAT is the BCAT developed by Dreyfus et al.[12] Multiple comparisons of these surgical techniques have been conducted to date,[13–17] most of which favor the BCAT because the well-maintained RA architecture and function (contraction) reduces the incidence of TVR.

The hemodynamic and echocardiographic data for our patients undergoing the mBCAT resembled those previously reported for the original BCAT.[13–17] The values for RA, right ventricular, pulmonary arterial and pulmonary capillary wedge pressures in our series agreed with those obtained after BCAT and reported by El-Gamel et al,[13] Aziz et al,[14] Traversi et al,[15] and Sun et al.[16] The RA pressure was always lower with the BCAT than with the BAAT. The increased late diastolic tricuspid flow (52±19 cm/s) in the present patients after the mBCAT was similar to that with the BCAT (48±18 cm/s) reported by Sun et al[16] and clearly indicated more vigorous RA contraction followed by better RA and right ventricular relaxation with the BCAT or mBCAT. Also, the E/A ratio of tricuspid flow in our patients (1.4±0.6) was close to that with BCAT in Traversi et al's series (1.2±0.5).[15] The incidence of moderate to severe TVR was as low as 5%, with a mean grade of 1.5±0.8 (range 0–3), and that of mitral regurgitation was essentially none, and there has been no requirement for pacemaker implantation in any of the patients from this series. Accidental chordal damage of the tricuspid valve at the time of endomyocardial biopsy is an important causative factor for significant TVR, and occurred in 1 patient in this series, causing acute onset of grade 3 TVR (5%). The biopsy specimen contained a piece of the chordal tissue. Otherwise, the grade of TVR has been mild and stable to date in this series.

The adverse impact of significant TVR on mortality or the need for re-transplantation has also been stressed in pediatric heart transplantation,[18] and prophylactic donor tricuspid annuloplasty by the DeVega method in order to prevent post transplant TVR was recently reported to be effective in decreasing cardiac-related mortality.[19] In addition, some previous articles[15,16,19] strongly suggested benefits of the BCAT that contribute to a reduction in long-term cardiac-related mortality. However, 2 recent papers dealing with the same subject either by conducting a systemic review and meta-analysis[20] or by analyzing the UNOS database[21] reached a similar conclusion, namely, that both the BCAT and BAAT lead to equivalent survival, and that the long-term beneficial effects, such as exercise capacity and health-related quality of life, remain to be evaluated. Nevertheless, both reports again admit the clinically relevant beneficial effects of the BCAT in comparison with the standard BAAT.

Although this was an observational study and it is difficult to demonstrate the superiority of the mBCAT compared with the original BCAT, which was performed in only 1 patient[2] not included in this series, clinical outcomes, including the survival rate up to 8 years, were excellent with similar hemodynamic and echocardiographic results to those previously reported for the BCAT.[13–17] With this modified technique, there have been no adverse effects attributable to

leaving a strip of the posterior wall of the right atrium. The mBCAT has been accepted as an easy alternative in nearly 70% of orthotopic heart transplantation in Japan.[4] The mBCAT can prevent some technical disadvantages encountered with the original BCAT, such as shrinkage, retraction and distortion of the SVC and IVC, with no additional operating time required. Moreover, we often found that the anastomosis could be carried out with ease in cases of mismatched donor–recipient hearts because we could create a large anastomotic orifice by expanding the suture line into the preserved posterior wall of the right atrium when the donor heart was large or we could easily adjust the distance between the SVC and IVC when the donor heart was small. There have been no episodes of caval anastomotic stenosis[22] in our series. In conclusion, this modification further facilitates techniques for transplantation with the same hemodynamic and echocardiographic benefits as with the original BCAT.

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