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A Modified Technique and Hemodynamic Evaluation of Heterotopic Cardiac Transplantation (Modified Ide Method)

Taijiro SUEDA[1], Yuichiro MATSUURA[1], Takeshi MATSUSHIMA[1] and Hiroki KAJIHARA[2]

1) The First Department of Surgery, Hiroshima University School of Medicine, Hiroshima 734, Japan
2) The First Department of Pathology, Hiroshima University School of Medicine, Hiroshima 734, Japan

ABSTRACT

A model of heterotopic cardiac transplantation which can evaluate the donor's heart function after preservation was developed. This model was modified from the working double heart model developed by Ide and his associates and is characterized by its ease in suturing in donor and recipient hearts.

Five mongrel dogs with the donor heart were observed hemodynamically from 3 to 6 hrs. Systemic circulation was successfully maintained with only the donor heart after ligation of the recipient aorta.

This working double heart model consists of total LV bypass and partial RV bypass, and therefore permits estimation of LV function of the donor heart.

Key words: *Heterotopic cardiac transplantation, Myocardial preservation*

Since the initial report of cardiac transplantation by Carrel and Guthrie[2] in 1905, a good number of experimental transplant surgeries have been attempted. In these early procedures[5,8], the donor's heart was anastomosed to the recipient's carotid artery, iliac artery and abdominal aorta for evaluation of the healing of vascular anastomosis and for physiological observation of the denervated heart and the rejection process.

The experimental work of Lower and Shumway[5] provided an acceptable basis for this transplant surgery and the first clinical application was performed by Barnard[1] in 1967. Orthotopic cardiac transplantation remains the standard procedure for clinical cardiac transplantation in patients with end-stage heart disease. Orthotopic grafting might be ideal in experimental cardiac transplantation. However, this method requires costly extracorporeal circulation and has the disadvantage of causing excessive surgical damage to the recipient and resulting in short postoperative survival. A number of potential advantages of heterotopic cardiac transplantation have been shown[7]. Heterotopic grafting does not require extracorporeal circulation nor heparin[9]. In addition, the heterotopic grafting method developed by Ide and his associates can maintain systemic circulation with only the donor's heart and has been named working double heart. The authors modified this heterotopic grafting method and simplified the operative procedure. This paper describes the operative procedure and presents the hemodynamic observation of this modified heterotopic cardiac transplantation.

MATERIALS AND METHODS

Studies were performed on five pairs of mongrel dogs weighing 11 to 23 kg. Donor heart was implanted in the left thorax by heterotopic transplant method.

(1) Donors

Animals weighing 10 to 15 kg were anesthetized with ketamine (10 mg/kg) and succinylcholine chloride (1 mg/kg) and then mechanically ventilated. After left fourth intercostal thoracotomy, the brachiocephalic vessels and proximal descending aorta (approximately 4 cm in length) were mobilized widely and several intercostal arteries were divided. A cannula was inserted proximally through the left innominate artery. The right innominate artery and distal left innominate artery were ligated and divided. The superior vena cavae and azygos vein were ligated and divided and a long segment of the inferior vena cavae was mobilized. After aspiration of blood from right appendage, the inferior vena cavae was occluded and the proximal descending thorcic aorta was clamped. Cold cardioplegic solution (4°C Bretschneider's solution, 20 ml/kg) was injected through the left innominate arterial cannula. The main pulmonary artery was transected and the pulmonary veins were isolated and divided. The heart was removed and immersed in iced lactate Ringer's solution.

Address: Mr. Taijiro Sueda M.D., 1-9-3-1013, Ujina Miyuki, Minami-ku, Hiroshima 734, Japan

(2) Recipients

Recipient dogs weighing 11 to 23 kg were anesthetized with intramuscular ketamine (10 mg/kg) and intravenous succinycholine chloride (1 mg/kg) and then ventilated mechanically. The left femoral vein was cannulated with the infusion line. The left common carotid artery and left external jugular vein were isolated and the cannulas were inserted for measurement of arterial and central venous pressure.

(3) Anastomotic procedure

Thoracotomy was made in the left forth intercostal space. After pericardiotomy, the left appendage and left pulmonary vein were isolated. The aortic arch and pulmonary trunk were also isolated and encircled with teflon tape. A short piece of the descending aorta of the door (3 cm in length) was resected and the proximal end of this piece was anastomosed to the inferior vena cavae of the recipient with 5-0 polypropylene (Fig. 1).

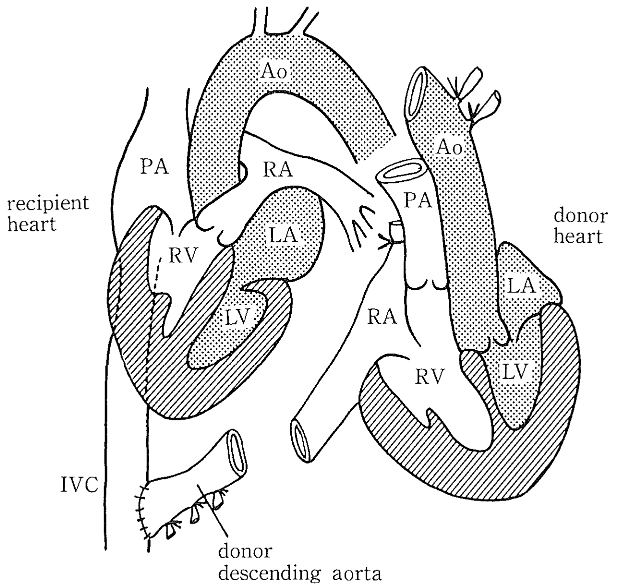

Fig. 1. Anastomotic procedure of heterotopic cardiac transplantation (1)
A short piece of donor descending aorta was anastomosed to IVC of the recipient heart.

The left atrium of the donor was anastomosed to the left appendage of the recipient with 4-0 polypropylene. An anastomotic area was made as wide as possible. After completion of left atrial anastomosis, the clamp was dislocated toward the proximal portion of the donor's left atrium and bleeding was checked and controlled. Then the pulmonary trunk of the donor was anastomosed to the left pulmonary artery of the recipient with 5-0 polypropylene. Above mentioned procedure is almost the same one of Ide method[4].

Descending aorta of the donor was anastomosed to the descending aorta of the recipient with 5-0 polypropylene. Finally, the inferior vena cavae of the donor was sutured to the distal end of the piece of the descending aorta which had been previously anastomosed to the inferior vena cavae of the recipient. This suture technique was developed by the author and easier to anastomose IVC of the donor to IVC of the recipient.

Before the occlusion clamp on the aorta of the donor was released, the clamp on the left atrium and pulmonary artery was released and air was aspirated from the left innominate artery and right appendage. Manual cardiac massage was commenced for resuscitation of the donor heart following slow release of aortic clamp on the donor aorta. After defibrillation of the donor heart, both hearts commenced their beats and were retained for 30 min in the condition of bi-ventricular bypass. When contractility of the donor heart recovered vigorously, the ascending aorta of the recipient was ligated (Fig. 2).

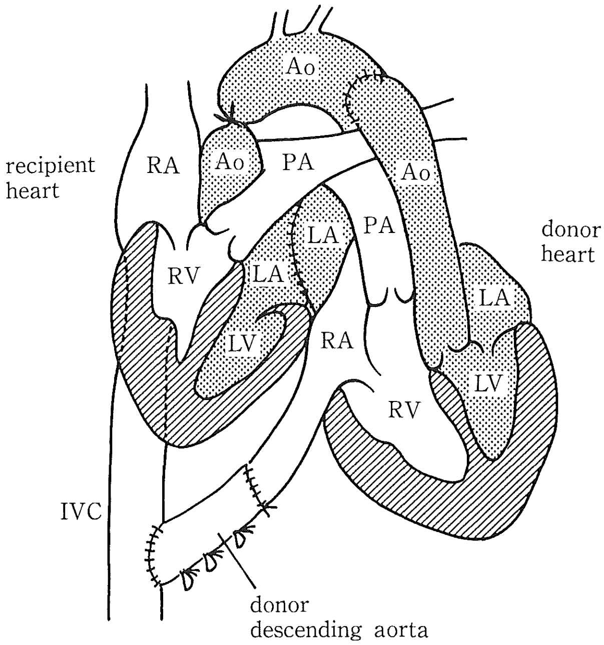

Fig. 2. Anastomotic procedure of heterotopic cardiac transplantation (2)
After the donor heart vigorously recovered, the ascending aorta of the recipient was ligated. Systemic circulation could be maintained only by the donor heart.

Arterial pressure (AP) of the recipient, left ventricular pressure (LVP) of the donor, LV max dp/dt of the donor and LVP of the recipient were measured continuously for 3 to 6 hrs by a high-fidelity pressure monitoring catheter inserted into each ventricle and artery.

RESULTS

All the donor hearts recovered their spontaneous beating with regular rhythm and gained vigorous contraction. The average cold preservation time of the donor heart was 142 min (112 ~ 183 min). During myocardial preservation, temperature of graft myocardium remaing in 0—6°C by iced saline. Graft anastomosis required approximately 50 min

No of dog	Sex	B. W.	Observation Time
1	♂	13.5	3 hrs
2	♂	11.0	3.5 hrs
3	♀	23.0	6 hrs
4	♀	11.5	3.5 hrs
5	♀	12.0	3 hrs

Fig. 3. Objects of heterotopic cardiac transplantation

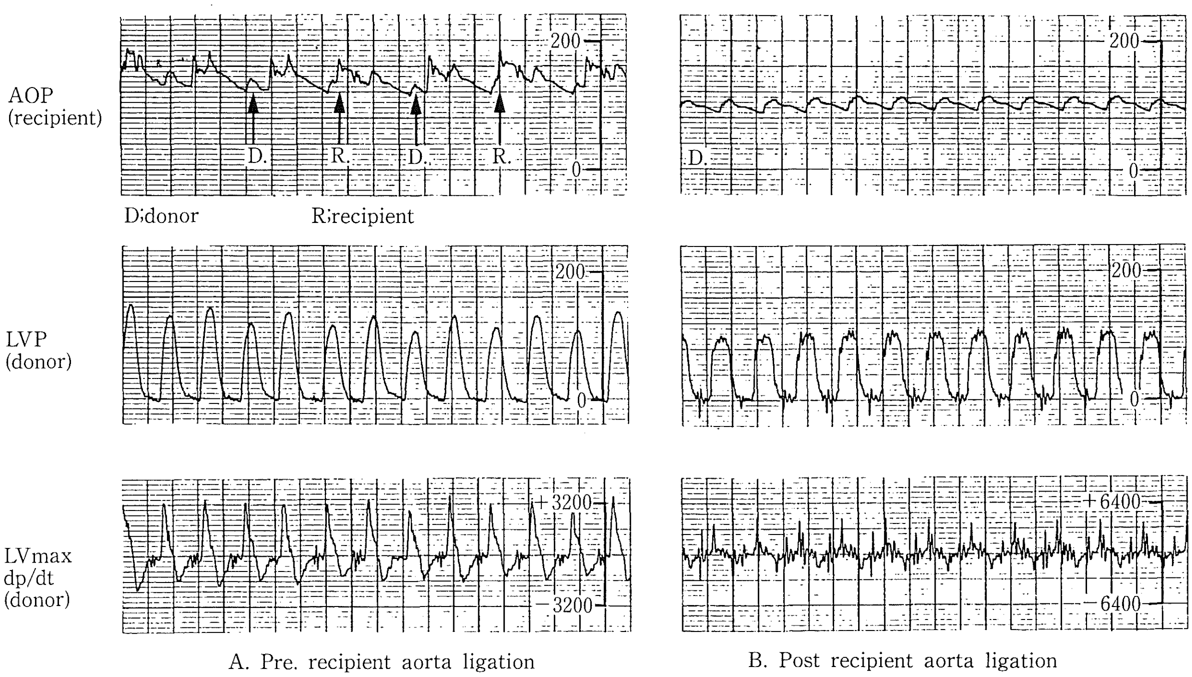

Fig. 4. Hemodynamic change of heterotopic cardiac transplantation
Biphasic arterial pressure including AOP of the donor and recipient hearts was recognized before aortic ligation. AOP and LVP of the donor heart decreased slightly, but LV max dp/dt increased a little after aortic ligation.

in room temperature. After resucitation of the donor hearts, hemodynamic observation could be continued for 3 ~ 6 hrs (average 4 hrs) (Fig. 3) and then all dogs were sacrificed for pathological study.

Left ventricular and arterial pressure measurements were conducted for 3 hrs. Electrocardiogram showed biventricular rhythm and the QRS complex of the auxillary heart could be easily identified on the standard limb leads. Arterial pressure of the recipient usually exceeded that of the donor before aorta ligation (Fig. 4).

When the ascending aorta of the recipient was ligated, arterial pressure fell from 152 mmHg to 102 mm, but thereafter the decrease of arterial pressure after clamping of the ascending aorta of the recipient diminished and the donor heart could maintain systemic circulation with the aid of blood transfusion (Fig. 5).

LVP of the donor heart elevated slightly after aorta ligation and LV max dp/dt also elevated after electrolyte infusion. LVP of the recipient heart increased twohold after aorta ligation, increasing from 100 mmHg to 200 mmHg, but this increase of LVP tended to gradually decrease with time. One of the five recipient hearts developed ventricular fibrillation during the observation period.

Mismatch in size between the donor heart and recipient heart was one of the important problems. The donor heart could not maintain the systemic circulation of the recipient in size-mismatch experiments of dog No. 3, and arterial pressure dropped

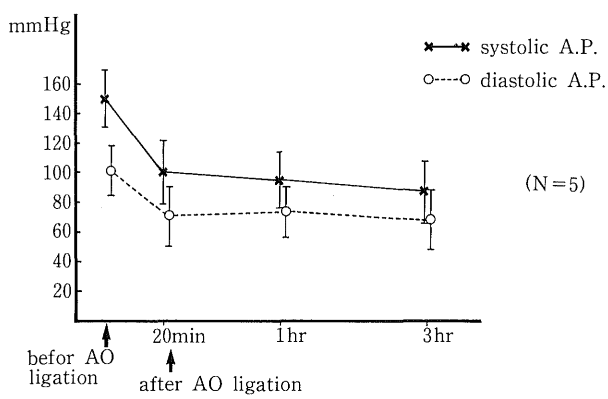

Fig. 5. Systemic pressure change after ligation of the recipient aorta in heterotopic cardiac transplantation. Donor heart could maintain the systemic pressure of the recipient to 90—100 mmHg after recipient aortic ligation.

as low as 80 mmHg after ligation which could not be elevated even by blood transfusion (Fig. 6).

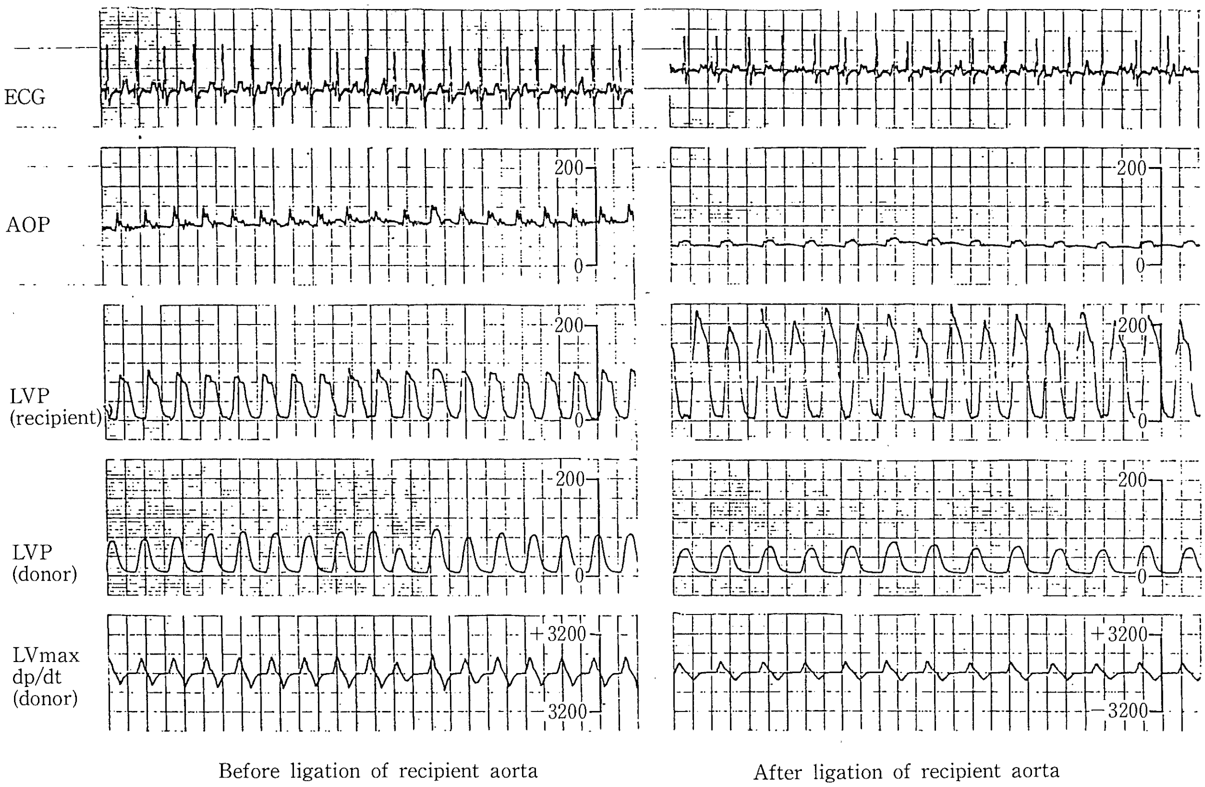

Fig. 6. Hemodynamic change before and after the ligation of recipient aorta.
LVP of the recipient after aortic ligation increased more than twice the pressure level prior to aortic ligation. LVP and LV max dp/dt of the donor heart decreased slightly after aortic ligation. Low AOP was attributable to mismatch in size between donor and recipient hearts in this case.

DISCUSSION

The heart is one of the first organs to be transplanted. In 1905 Carrel and Guthrie[2] described two heterotopic cardiac transplants which had functioned for several hours. Thereafter, Mann and his associates[5] developed the technique of heterotopic cardiac transplantation in which the donor heart was transplanted in the neck of the recipient. This technique has been used extensively in pathologic, immunologic, and biochemical studies on cardiac transplantation.

Intrathoracic transplantation of the heart was introduced by Demikhok. The studies of Lower and Schumway[5] demonstrated unequivocally that the transplanted heart could completely support the circulation of the recipient and survival for one year was obtained following in situ replacement of the transplanted heart. In situ replacement involves extracorporeal circulation and excision of the recipient heart, but these procedures impose certain difficulties in animal experiments. Extracorporeal circulation is expensive and requires heparin. Furthermore, hemostasis after excision of the heart is somewhat troublesome, resulting sometimes in unsuccessful transplant. Heterotopic transplantation, at least in these points, is considered to have several advantages[7] over orthotopic transplantation. In particular, the working double heart model developed by Ide and his associates[4] has several potential advantages, such as no need for heparin and extracorporeal circulation, successful evaluation of hemodynamics, and acute rejection of the donor heart. However, one of the disadvantages of this model is the difficulty involved in suturing the donor's IVC to the recipient's IVC. The authors has therefore modified this model to make the surgical procedure simple and experimentally evaluated its effectiveness, especially to ascertain that the piece of donor aorta is sufficient for the conduit of venous return. Hemodynamically, the donor hearts could maintain the systemic circulation and surgical procedure seemed to be easier than the original one. So this modification may have some adventage.

LVP of the recipient heart showed interesting hemodynamic changes after aortic ligation. LVP of the recipient heart increased twofold over the usual pressure after aortic ligation and thereafter decreased gradually. It was assumed to reach the pressure level prior to aortic ligation. Though this short observation provided some speculation on the fate of the recipient heart, the left ventricular myocardium of the recipient may change pathologically to hypertrophic cardiomyopathy in the future.

One of the five recipient hearts developed ventricular fibrillation after aortic ligation. The mortality was attributable to the elevated pre-load and after-load for the recipient left ventricle. A solution for this might be to enlarge the anastomosis of the left atrium in order to diminish pre-load of the recipient left ventricle and increase pre-load of the donor left ventricle.

Working double heart model is not a perfected model of transplant grafting from the hemodynamic point of view. The donor heart consists of complete left ventricular bypass and partial right ventricular bypass and recipient heart provides right ventricular assistance to the donor heart[4]. So the authors have also developed another form of heterotopic cardiac transplantation. Another heterotopic transplant model works as complete left ventricular bypass and complete right ventricular bypass formed by both aortic and pulmonary ligation.

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