

## Experience in Heart Transplantation after Dynamic Cardiomyoplasty

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**We report a case undergoing heart transplantation due to gradual progression of heart failure four years and one month after dynamic cardiomyoplasty. This case reports a 61-year-old man who received drug therapy after being diagnosed as having idiopathic dilated cardiomyopathy, but his heart failure progressed to New York Heart Association (NYHA) class III-IV, and heart transplantation was thought to be indicated. However, dynamic cardiomyoplasty was performed because this patient rejected heart transplantation. An implantable cardioverter/defibrillator (ICD) was implanted for postoperative ventricular arrhythmia. After that, his symptoms rapidly improved, but his heart failure gradually worsened two years after surgery and heart transplantation was performed four years and one month after dynamic cardiomyoplasty. Since transplantation he has had an uneventful postoperative course without rejection or complications. (Ann Thorac Cardiovasc Surg 2002; 8: 319–22)**

**Key words:** heart transplantation, dynamic cardiomyoplasty

### Introduction

Prognosis of end-stage heart failure still remains extremely poor, despite advances in drug therapy, such as angiotensin-converting enzyme (ACE) inhibitors and beta-blockers. Heart transplantation has been considered as the gold standard method for end-stage heart failure. Although outcome of heart transplantation is stable due to advances in immunosuppressions, less than 10% of patients awaiting transplant can actually have a transplant due to donor organ shortage. For this reason, recently various surgical treatments (volume reduction surgery, mechanical circulatory support, dynamic cardiomyoplasty, myocardial revascularization for severe left ventricular dysfunction, transmyocardial laser

revascularization (TMLR) and biventricular pacing) have been actively performed.<sup>1)</sup>

We describe a case undergoing heart transplantation due to gradual progression of heart failure, despite implantation of an implantable cardioverter/defibrillator (ICD) for ventricular arrhythmia and heart failure following dynamic cardiomyoplasty.

### Case Report

The case reports a 61-year-old man who was being followed up at another hospital under the diagnosis of idiopathic dilated cardiomyopathy. However, his heart failure progressed to New York Heart Association (NYHA) class III-IV, despite maximum drug therapy, ventricular ejection fraction was 18%, left ventricular diastolic diameter was 72 mm by echocardiography, and heart transplantation was thought to be indicated. However, dynamic cardiomyoplasty was performed by the same hospital in November 1996 because this patient rejected heart transplantation. An ICD was done in December for postoperative ventricular fibrillation and ventricular tachycardia. Although mild symptoms of heart failure appeared with low stress after surgery, he had rapidly improved several

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months after surgery, and he could restore his dialy activities without difficulty. However, symptoms of heart failure gradually reappeared two years after cardiomyoplasty, showing no response to beta-blockers or ACE inhibitors. His general condition worsened in January 2000. Severe left ventricular dysfunction was recognized by echocardiography (LVDD, 80 mm; EF, 25%) and short atrial fibrillation occurred frequently. Additional administration of an antiarrhythmic therapy failed to improve his symptoms. Thus he was referred to our institute for heart transplantation in November of the same year. At admission, his heart failure progressed to NYHA class IV; marked left ventricular dilatation and severe ventricular dysfunction were recognized by echocardiography (LVDD, 92 mm; EF, 25%). Thus he was determined to be a candidate for heart transplantation and registered on the Eurotranplant list. On December 18, 2000, heart transplantation was performed using a conventional procedure (Lower and Shumway's procedure) without difficulty. Adhesion between the heart and the latissimus dorsi muscle (LDM) flap was not released, and the heart and the LDM were resected en bloc. The operation time was 251 min, cardiopulmonary bypass time was 114 min, aortic cross clamping time was 69 min, and ischemic time of donor heart was 202 min. The recipient's heart had markedly dilated right and left ventricles and was as heavy as 714 g, clearly demonstrating the features of end-stage dilated cardiomyopathy. The LDM was markedly atrophic and thin. Although the LDM should have been primarily wrapped around the heart, completely covering the right ventricle, this muscle graft only reached the area up to the left anterior descending artery (LAD) in the left ventricle. Histopathologically, lipoma-like atrophic lesions and fibrosis were observed in the LDM, indicating a very severe degree of muscular atrophy. There was no neovascularization seen in the epicardial-muscle interface.

After heart transplantation, he showed an uneventful course, and was discharged 32 days after transplantation. At the present time, four months after transplantation, he has been in a good condition without rejection or complications.

## Discussion

Recently, heart transplantation has provided stable long-term outcome with introduction of cyclosporine and mono- and polychronal antibodies, and so on.<sup>2)</sup> It is the currently most effective therapeutic method for end-stage heart failure. However, heart transplantation has some

problems, including the shortage of donor heart, rejection, and complication of immunosuppression. In recent years, the effectiveness of ventricular assist devices (VAD) for end-stage heart failure and long-term support with VAD over two years have been reported.<sup>3,4)</sup> However, VAD may cause complications, such as thromboembolism, infection, and mechanical failure, which become more remarkable as the duration of support is prolonged.<sup>3)</sup> Assist devices available for permanent use (longer than five years) are not available.

Since dynamic cardiomyoplasty was first performed by Carpentier and Chachques in 1985,<sup>5)</sup> more than 1,000 cases have been treated worldwide.<sup>6)</sup> Because two months are required to condition the transposed LDM to induce fatigue resistance, dynamic cardiomyoplasty cannot provide immediate postoperative improvement of cardiac function. Although dynamic cardiomyoplasty has this shortcoming, it is free from complications caused by immunosuppression or from thromboembolism. Recently, long-term clinical results of this method have been reported from many institutes.<sup>7-13)</sup> (Table 1) Chachques et al. reported that the actuarial survival rate at seven years was 54% in all patients, and 66% for patients who underwent cardiomyoplasty in NYHA class III. However, results of patients in NYHA class IV were poor, the actuarial survival rate at seven years was 22%. They concluded that patient selection was the most important determinant.<sup>10)</sup> At the present time, clinical trials have been conducted under the control of the Food and Drug Administration (FDA).<sup>14)</sup> In a phase I trial, the hospital mortality was found to be as low as 12% in NYHA class III patients, but as high as 33% in class IV patients.<sup>7)</sup> Therefore, NYHA class IV patients have not been included as candidates for this method in phase II and III. As a result, the hospital mortality was 12% in a phase II trial,<sup>9)</sup> and the hospital mortality in the ongoing phase III trial has been reported to be less than 3%.<sup>14)</sup> Although the systolic assist, such as increases in left ventricular ejection fraction and cardiac output, was first thought to be the mechanism of action of dynamic cardiomyoplasty, it has been reported that the systolic capacity of the left ventricle can be maintained at an improved level for three years after cardiomyoplasty, but at the preoperative level after that period. However, maintenance of the improved clinical symptoms has also been reported. Further, it has been reported that the left ventricular ejection fraction does not always reflect the improved degree of clinical symptoms.<sup>8)</sup> Beneficial effects of dynamic cardiomyoplasty are now considered to be induced by various mechanisms of

**Table 1. Results of dynamic cardiomyoplasty in the literature**

Author	Patient No.	Hospital mortality	Survival rate
Grandjean et al. <sup>7)</sup> (Phase I trial, 1991)	74	22% NYHA III: 12% NYHA IV: 33%	NYHA III: 1.5 y: 75% NYHA IV: 1.5 y: 42%
Moreira et al. <sup>8)</sup> (1995)	31	0%	2 y: 61.4% 3-5 y: 42.5%
Furnary et al. <sup>9)</sup> (Phase II trial, 1996)	68	12%	1 y: 68%
Chachques et al. <sup>10)</sup> (1997)	82	NYHA III: 10% NYHA IV: 36%	7 y: 54% NYHA III: 66% NYHA IV: 22%
Tasdemir et al. <sup>11)</sup> (1997)	24	20.8% Ischemic : 36.3% Idiopathic: 7.6%	2 y: 71% Ischemic: 55% Idiopathic: 85%
Lorusso et al. <sup>12)</sup> (1997)	22	4.2%	4 y: 69.7%
Braile et al. <sup>13)</sup> (2000)	52	9.6%	Non-Chagas disease: 5 y: 49.9%; 9.2 y: 14.9% Chagas disease: 4 y: 12.5%; 5 y: 0%

action, other than the systolic assist, including limitation of ventricular dilatation, ventricular remodeling with an active girdling effect, reduction of ventricular wall stress (sparing effect), angiogenesis, and a neurohumoral effect.<sup>6)</sup>

As for causes of death after dynamic cardiomyoplasty, heart-related deaths, particularly frequent sudden deaths due to arrhythmia have been observed. Thus implantation of an ICD has recently been recommended to prevent sudden death caused by arrhythmia.<sup>15)</sup> Reports on heart transplantation after dynamic cardiomyoplasty have rarely been published. Chachques et al. reported that heart transplantation was performed on 5 of 82 patients after dynamic cardiomyoplasty, because of refractory heart failure. However, three of the five patients respectively died of graft failure at 7, 18, and 60 months after transplantation. They defined the following two indications for heart transplantation after dynamic cardiomyoplasty: 1) early indication in patients in whom LDM contraction was never sufficient in assisting ventricular function; 2) after a period of improvement, when the patient's clinical status deteriorates as a result of the natural evolution of the underlying myocardial disease.<sup>10)</sup> At our institute, we do not conduct dynamic cardiomyoplasty, and we very rarely perform heart transplantation after dynamic cardiomyoplasty. Among 1,122 patients receiving heart and heart/lung transplantation at our institute between 1989 and 2000, only two patients (0.18%), including the one described in this article, underwent heart transplantation after dynamic cardiomyoplasty. Another case was

a 37-year-old man who had NYHA class III idiopathic dilated cardiomyopathy with a 15% ejection fraction, and had undergone dynamic cardiomyoplasty at another hospital. His cardiac function showed almost no improvement after cardiomyoplasty, and he was referred to our institute two years after the surgery. Heart transplantation was performed 2.5 years after cardiomyoplasty. He has shown an uneventful posttransplantation course without rejection or complications at the present time, 3.5 years after transplantation. Since these two cases we encountered had poor preoperative cardiac function and detrimental clinical statuses, we cannot exclude the possibility that dynamic cardiomyoplasty should not have been indicated for them.

Misawa et al. reported histopathological features of the LDM after dynamic cardiomyoplasty, found at autopsy in five cases dying one month to six years after dynamic cardiomyoplasty, and they observed a limited clinical response in two of the five cases. One case was that the LDM showed atrophic edematous appearances associated with fatty infiltration; the other one was that the LDM wrapped around the dilated heart was insufficient in length.<sup>16)</sup> Our patient also showed histopathological and macroscopic appearances resembling those of the cases reported by Misawa et al.<sup>16)</sup> Although we do not know about the details of dynamic cardiomyoplasty associated with the patient reported because he had received the cardiomyoplasty at another institute, we cannot exclude the possibility that the LDM had not been sufficiently

wrapped around the right and left ventricles because of predominant heart dilatation at the time of dynamic cardiomyoplasty.

At the present time, it is difficult to state the indication of dynamic cardiomyoplasty. We cannot state the indication because of no experience on the dynamic cardiomyoplasty in our institute. However, based on results from an on-going clinical trial managed by FDA and from previous reports, the dynamic cardiomyoplasty may be indicated for NYHA class II or III patients controlled to some extent by medication since training of the LDM takes two months, but it may be unsuitable for NYHA class IV patients. Now surgical therapies for end-stage heart failure includes VAD, volume reduction surgery and biventricular pacing. It is essential to the treatment of end-stage heart failure that an adequate therapeutic method is selected from various currently available surgical methods. These new surgical methods will decrease the number of patients who require heart transplantation, leading to the effective utilization of a limited number of donor hearts, and subsequently increasing the survival rate in patients with end-stage heart failure. In the future, cooperation with other therapeutic methods, such as dynamic cardiomyoplasty, VAD and volume reduction ventriculectomy will be needed to achieve heart transplantation successfully.

This case finally required heart transplantation because his heart failure could not be improved using an ICD after cardiomyoplasty. However, dynamic cardiomyoplasty seemed to serve as an effective bridge to heart transplantation in our patient while various treatments were selected under careful follow-up. Thus our patient is thought to represent an interesting case indicating a potential role of dynamic cardiomyoplasty.

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