

# Surgical Treatment for Severe Heart Failure: Recent Progress in Treatment Strategy and its Present Status in Japan

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**Chronic intractable heart failure that is unresponsive to maximum medical therapy can have a wide variety of causes; these include advanced valvular diseases and severe myocardial ischemia, ischemic cardiomyopathy (ICM) in heart failure following extensive myocardial infarction, chronic heart failure due to dilated cardiomyopathy (DCM) in which the myocardium itself is progressively damaged or the acute aggravation of the latter. Heart transplantation has long been considered the only useful treatment for patients with heart failure due to ICM- and DCM-induced severe left ventricular hypofunction. However, because of the extremely limited number of heart transplant donors, other surgical treatments have also been attempted. In this communication, we provide an overview of the current situation with regard to left ventriculoplasty and heart transplantations, as well as of the treatment of severe heart failure using ventricular assist devices, which have recently shown remarkable progress.**

**Key words:** heart transplant; left ventriculoplasty; ventricular assist device

Chronic intractable heart failure that is unresponsive to maximum medical therapy can have a wide variety of causes. These include advanced valvular diseases; severe myocardial ischemia; ischemic cardiomyopathy (ICM), which is a state of chronic heart failure that develops after an extensive myocardial infarction; and dilated cardiomyopathy (DCM), which is heart failure due to the failure of myocardial cells. Heart transplant has long been considered the only treatment for patients with heart failure due to severe left ventricular functional decline resulting from ICM and DCM. However, because of the very limited number of heart transplant donors, other surgical treatments have also been attempted. Left ventriculoplasty is one such treatment that involves adjusting the shape, reducing the volume, and improving the function of the

left ventricle, whose lumen is enlarged because of heart failure. It has been clinically applied for the treatment of ICM since the 1980s (Dor et al., 1995), and its indication has also spread to the treatment of DCM since the 1990s (Batista et al., 1996). However, the limitations of these surgical procedures have been gradually revealed in recent years, and continual efforts have been made to improve surgical methods and to establish their indications (Suma and RESTORE Group, 2001; Matsui et al., 2004).

Since the establishment of the Organ Transplant Law in 1997, heart transplantation from brain-dead patients has also been performed in Japan. However, the law strictly required that in order for organs to be transplanted, the donors had to express their intent to donate their organs when alive; consequently, 10 years since the enforcement of the law,

Abbreviations: DCM, dilated cardiomyopathy; ICM, ischemic cardiomyopathy; LVAD, left ventricular assist device; QOL, quality of life; NYHA, New York Heart Association; MR, mitral regurgitation; SAVE, septal anterior ventricular exclusion

the number of brain-dead donors has been approximately 60, which, in a population of 100 million people, was the equivalent of 5 brain-dead donors per year, in other words, 100 times less than the number found in Western countries. Under such circumstances, the revised version of the Organ Transplant Law was enacted in 2010, and organ donation from a brain-dead patient has become possible upon obtaining consent from the patient's family members, even in the absence of a declaration of intention provided by the patient before death. Therefore, the number of heart transplants performed has increased to 50 per year. However, the number is still only about one-tenth of that in Western countries and thus is still insufficient. In the 1990s, left ventricular assist devices (LVADs) were actively used as a bridge in heart transplantation. In particular, implantable LVADs such as HeartMate (Thoratec, Pleasanton, CA) and Novacor (WorldHeart, Ottawa, Canada) have been widely used in Europe and the United States because of their capability to provide a better long-term quality of life (QOL). The practical use of small-sized and long-term durable continuous-flow pumps in clinical settings was initiated in 2000. Therefore, the survival rate has improved, and destination therapy has been attempted on patients who are not candidates for heart transplantation. In addition, there have been reported cases in which the patients' own cardiac function recovered after using VADs for circulatory support, which enabled these patients to withdraw from these VADs (bridge to recovery); this has attracted attention as a new possibility (Müller et al., 1997).

The present report provides an overview of the current situation regarding the surgical treatment of severe heart failure.

### **Left ventriculoplasty for the treatment of ischemic cardiomyopathy**

#### **Concept**

Resection of left ventricular aneurysms to treat the extensive dyskinesia that can occur after a trans-

mural myocardial infarction was first performed by Cooley in 1958 under artificial heart and lung support; many later studies have shown its effectiveness. Dor et al. reported, beginning in the 1980s, that even in treatment of ICM (which causes an overall decrease in left ventricular function because of extensive akinesis), left ventriculoplasty was also believed to improve cardiac function, in the same manner as in its use in the treatment of left ventricular aneurysms (Dor et al., 1995). Because of the spread of early intervention in the treatment of acute myocardial infarction, the number of patients with persistent akinesis due to subendocardial infarctions tends to be higher than that due to transmural infarctions. However, after a relatively extensive myocardial infarction, and regardless of whether the infarcted region shows dyskinesia or akinesis, a remodeling occurs, causing a gradual expansion of the noninfarcted region along with deterioration in its function. Ultimately, this leads to ICM, namely, a decrease in the contractility of the entire left ventricle. In such cases, left ventriculoplasty is applied that aims to improve both the contractility of the remaining noninfarcted region and the left ventricular dilatation and morphological changes caused by the remodeling during surgical resection or plasty of the infarcted region.

#### **Surgical procedure**

The problem with the conventional surgical technique (a method known as "linear closure", which consists of performing a longitudinal incision in the infarcted region in the anterior wall of the left ventricle, with resection and suturing of the infarcted area) is that the infarcted region remains in the septum; therefore, Dor et al. proposed a method consisting of a purse-string suture (a Fontan stitch) at the infarction site, including the septum and its border with healthy areas, followed by closure through application of a patch (Dor et al., 1995). Ever since its introduction, the method has been widely used worldwide. In addition, the surgical technique known as septal anterior ventricular exclusion (SAVE), in which a vertical patch is sewn at

the border between the infarcted area and healthy regions, has also been performed. In this technique, Fontan stitch is not required to ensure that the left ventricle has a shortened transverse diameter and an oblong shape (Suma and RESTORE Group, 2001). Both methods allow for a reduction in the volume of the left ventricle and make it possible to ensure that the morphology of the left ventricle (which becomes spherical due to remodeling) returns to its original oblong shape.

### **Indications and outcomes**

The indications for this surgical technique include the presence of symptoms such as heart failure, chest pain, and arrhythmia; akinesis or dyskinesis over a broad region (occupying 35% or more of the left ventricular circumference) due to anteroseptal myocardial infarction; and expansion of the left ventricle (left ventricular end-diastolic volume index greater than 100 mL/m<sup>2</sup> or left ventricular end-systolic volume index greater than 60 mL/m<sup>2</sup>) and a decrease in left ventricular contractility (Menicanti et al. and RESTORE Group, 2002). Recently reported studies conducted in other facilities have shown that left ventriculoplasty has comparatively favorable outcomes. Surgical patients who met the above-mentioned indications have been reported to account for 1,198 cases, with a hospital mortality rate of 5.3%, a 5-year survival rate of 68.6%, and a 78% avoidance of heart failure at 5 years after surgery (Athanasuleas et al. and RESTORE Group, 2004). In addition, the efficacy of left ventriculoplasty in the treatment of mitral regurgitation (MR) has recently been the focus of attention. In ICM, which is often associated with left ventricular enlargement, annuloectasia and tethering of the mitral valve leaflets due to displacement of the papillary muscle cause reduction in the coaptation area and is often complicated by MR. Commonly, “undersizing and overcorrecting” by employing small-diameter full-circumference prosthetic valves enables restoration of the coaptation areas of the mitral valve leaflets and an improvement in MR. However, residual MR and recurrences often occur in patients with

severe tethering. During left ventriculoplasty, if sutures are also placed between the anterior and posterior papillary muscles for shortening the distance and restoring the mitral tethering from inside the left ventricle, the treatment was found to be more physiological and recurrences may be prevented (Menicanti et al. and RESTORE Group, 2004). Further, it has also been reported that in patients with a history of severe ventricular arrhythmias, the incidence can be reduced by cryocoagulation of the “gray zone” located at the borderline between the infarcted and noninfarcted regions, and the results comparable to those obtained using automated implantable cardioverter-defibrillators (DiDonato et al. and RESTORE Group, 2004).

## **Left ventriculoplasty for the treatment of idiopathic DCM**

### **Batista surgery**

In treatment of DCM, Batista first reported improvement in left ventricular contractility by reducing the left ventricular volume by performing a partial resection of the posterior wall of the left ventricle (Batista et al., 1996). Since then, the method has rapidly spread worldwide as “Batista’s surgery” (Batista procedure). The concept of surgical size reduction of the dilated left ventricle for preventing or reversing remodeling is similar to that used in ICM. However, the difference from the surgical treatment of ICM is that instead of the infarcted region, the remaining cardiac muscle with deteriorated function is removed.

### **Outcomes**

After Batista’s report, additional tests were conducted in Europe and the United States, and according to a report published by Cleveland Clinic on a study conducted on New York Heart Association (NYHA) class III or IV heart transplant candidates with a left ventricular end-diastolic diameter > 70 mm, the rate of patients who require heart trans-

plantation and assisted circulation because of acute circulatory failure was as high as 16%, and the rates of mortality and avoidance of recurrent heart failure at 1 year and at 3 years were 49% and 26%, respectively, which were considered low (Franco-Cereceda et al., 2001). Although the symptoms and left ventricular function certainly improved in some patients over time, such an outcome was difficult to predict preoperatively; therefore, this surgical technique was not performed in Europe and the United States. In Japan, because of the small number of heart transplant donors, the technique is performed as an alternative to heart transplantation in some institutions. Efforts aimed at improving outcomes continue and include the evaluation of local cardiac function before or during surgery, the resection of all regions showing poorest systolic contractions, rather than limiting the resection to only the posterior wall (Suma and RESTORE Group, 2001), and myocardioplasty in which the myocardium is left in place and is superimposed instead of resected (overlapping method) (Matsui et al., 2004).

### **Cardiac transplantation**

For more severe forms of heart failure in which no improvement is observed even after maximum medical treatment or after having been treated with the new surgical techniques described earlier, heart transplantation is the most effective method of treatment. One of the indications for heart transplantation is a diagnosis with a 2-year survival rate of about 50%. Meanwhile, patients treated by heart transplantation have a 2-year survival rate of 80% and a 10-year survival rate of 50%. Even from the perspective of malignant diseases, a 2-year survival rate of 50% suggests that a disease has quite a poor prognosis. Of the currently available treatments, heart transplantation is the one that can be expected to ensure the highest survival rate for such patients. Currently, approximately 3,000 patients per year undergo cardiac transplantation all over the world. In Japan as well, cardiac transplantation was officially initiated in 1997 after the establishment of

the Organ Transplant Law; however, because of various restrictions pertaining to organ donation from brain-dead patients, such as the strict application of the law requiring the donor to provide a written document stating their intent to donate organs before their death, very few people were able to receive heart transplants, and patients had to go through a long waiting period before undergoing cardiac transplantation. In response to that trend, the Revised Organ Transplant Law was enacted in 2010. Since the revised law was enforced, organ donation from brain-dead patients has become possible upon consent from their families, even if the patients themselves did not clearly show an intention to donate their organs before their death. In addition, organ donation from brain-dead children less than 15 years of age has also become possible. Since the enforcement of the revised law, organ donations from brain-dead patients have increased in number, and the number of cardiac transplantations performed per year has also increased, from 5 to 10 in the past to approximately 50. However, due to the increasing number of registered patients waiting for heart transplants, the changes did not lead to a shortening of the transplant waiting period.

Although cardiac transplantation is currently the most well-established therapeutic method for severe heart failure, it has also encountered various problems. One of which is the need for organ donation from brain-dead patients; the other is lifetime immunosuppressive therapy in most cases. Immunosuppressive agents are often expensive and impose a heavy financial burden on patients. In addition, the side effects of immunosuppressive agents are associated with various problems, including aggravation of arteriosclerosis and osteoporosis due to steroid use and an increase in carcinogenesis due to long-term suppression of immunocompetence. Therefore, efforts have been made to develop immunosuppressive drugs with fewer side effects. Given the problems associated with cardiac transplantation, treatment outcomes could be better if therapeutic methods are developed that provide a better vital prognosis than that associated with heart transplantation or which ensure an improvement in

QOL in a manner that outweighs that due to heart transplantation. Under such circumstances, treatments that use VADs have received attention.

### **Use of VADs for the treatment of heart failure**

#### ***The major VADs currently in use***

VADs, which began to be developed in the 1970s, have been used in clinical settings since the mid-1990s as bridges in heart transplantation. Some VADs are extracorporeal, and the others are intracorporeal. Those that were used in the 1990s were all pulsatile pumps. Because the types of pumps that are implantable inside the abdominal wall or inside the abdominal cavity are excellent in terms of QOL for patients wearing them, implantable pulsatile pumps have been widely used. The pumps were known as the first generation of implantable devices. In the early 2000s, the first-generation devices were found to have limitations such as the fact that the implanted portion was large, infections developed easily, and the mechanical durability of the devices was problematic. Therefore, the second and third generations of artificial hearts were developed. These have been successfully used in clinical settings. The new generation of devices consists of continuous-flow pumps such as axial-flow pumps and centrifugal pumps that are miniaturized. Their durability has also improved. The second-generation devices have a rolling-contact bearing of the rotor, and the third-generation devices have further improved durability and no longer have rolling-contact bearing. Previous reports have shown that because of the small size of the second-generation and third-generation VADs, surgery is less invasive and complications such as infection are less frequent (Frazier et al., 2004).

#### ***Pulsatile pumps***

Pulsatile pumps, which are known as the first-generation VADs, are of 2 different types: the paracorporeal type and the implantable type. Compared to the

paracorporeal VADs, implantable VADs generally have a blood pump implanted inside the body, such as in the abdominal region, and are therefore associated with a smaller risk of infection. In addition, because they are also excellent with regard to patient QOL, they are believed to be more suitable for long-term assistance lasting several months or more. Currently, the VADs that are most commonly used in Japan are the paracorporeal pumps manufactured by Nipro Corporation (Osaka, Japan) (Fig. 1).

When used for long-term assistance, paracorporeal pneumatically-driven VADs are associated with a poorer QOL than that allowed by the implantable type. However, like implantable pumps, they are useful as a bridge to heart transplantation. They are particularly useful for patients with a small physique whose body surface area is less than 1.5 m<sup>2</sup>, for pediatric patients, and for patients in need of bilateral ventricular assist system who, because of severe right heart failure, must be implanted with a VAD in the right ventricle in addition to that in the left ventricle. This is because the currently used implantable pumps have been designed to assist the left ventricle, and do not allow a second one to be implanted in the right ventricle. On the other hand, HeartMate (Thoratec) and Novacor (WorldHeart) are typical implantable pulsatile pumps (Fig. 2). Altogether, these 2 models have been used in more than 5000 cases worldwide; however, they have been rarely used since 2010 because continuous-flow pumps were found to be better.

#### ***Continuous-flow pumps***

Since the 1990s, active research and development has been done on the continuous-flow pumps such as implantable axial-flow pumps and centrifugal pumps. Their advantages include the fact that their size is smaller than those of conventional pulsatile pumps, they cost less because of their simple structure, and there is no need for artificial heart valves. Altogether, MicroMed DeBakey, HeartMate II (Thoratec), and Jarvik 2000 (Jarvik Heart, New York, NY; Fig. 3) have been used in clinical settings in more than 2000 cases in Europe and the United States. There has been a particularly exponential

**Fig. 1.** Nipro pneumatically-driven paracorporeal pump.

Left: pump is sit outside the body and connected to the console. The two cannulas penetrating the skin were connected to the left atrium and ascending aorta, respectively.

Right: a patient supported with Nipro pump. The patient is fully ambulated, but needs to go with the large consele next to him.



**Fig. 2.** Implantable pulsatile pumps. Two cannulas are connected to the left ventricle and ascending aorta, respectively. Pumps are sit either in the abdominal wall or in the abdominal cavity.

Left: Novacor (WorldHeart, Ottawa, Canada).

Right: HeartMate I (Thoratec, Pleasanton, CA).



**Fig. 3.** Jarvik 2000, an implantable continuous flow pump.

Left: Jarvik 2000 is shown on the palm. Note that the size is much smaller than those of the implantable pulsatile pumps.

Right: chest X-ray of a patient supported with Jarvik 2000. The pump itself is sit in the left ventricular cavity.



increase in the use of the HeartMate II, which has almost replaced the first-generation pulsatile pumps.

In Japan as well, 2 models of implantable centrifugal pumps, namely EVAHEART (Sun Medical, Suwa, Japan) and DuraHeart (Terumo, Tokyo, Japan), received approval for manufacture and sale in January 2011, and have been approved for insurance reimbursement since April 2011. HeartMate II (Thoratec) and Jarvik 2000 (Jarvik Heart) are also pending approval.

### ***New purposes of employing VADs “bridge to recovery”***

In 1990, when the use of VADs as a bridge towards heart transplantation became popular, it was believed that a VAD was installed in case of severe end-stage heart failure due to cardiomyopathy, which is a basically progressive disease, and therefore, withdrawal from the use of VADs was considered extremely difficult. However, in 1997, the Berlin Heart Institute reported that 17 patients with idiopathic DCM could withdraw from VADs, and the phenomenon attracted attention (Müller et al., 1997). A normalization of neurohumoral factors, an improvement of calcium handling in myocardial cells, and an increase in the number of beta adrenergic receptors are thought to occur while the cardiovascular circulation is assisted and the load on the heart is reduced by VADs. In Japan, where brain-dead donors are difficult to find, the “bridge to recovery” strategy is much more important than it is in Western countries, and its availability to all patients wearing VADs should be pursued. For all patients who undergo placement of a VAD in our institution, medical treatment of heart failure, consisting of the administration of medications such as beta-blockers and angiotensin-converting enzyme inhibitors, is initiated after the device has been put in place, as soon as the patient is capable of ingesting food and liquid orally. Recently, there has been a focus on strategies that aim at withdrawal from VADs by using methods that actively contribute to the recovery of left ventricular function in patients wearing the device; therefore, pharmacotherapy

and ventricular resynchronization, combined with surgical treatments such as mitral valvuloplasty, left ventricular reduction surgery, and regenerative treatments such as cell transplantation and gene therapy, have been reported to be useful (Nishimura et al., 2005). However, it is currently difficult to predict patients in which cardiac functional recovery is possible. In addition, future studies are expected to solve the issue of predicting or preventing the recurrence of heart failure after withdrawal from VADs and of evaluating the extent of recovery of cardiac function in patients wearing a VAD.

**Conclusion:** Although there have been remarkable developments in medical treatment for heart failure, surgery still plays an important role in its treatment, particularly in severe heart failure cases. In the future, combinations of a wider variety of therapeutic methods could be promising in improving treatment outcomes in severe heart failure.

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