Extracorporeal Assist Circulation for Heart Failure

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Acute cardiogenic shock has a high mortality, irrespective of the original etiology such as myocardial infarction, post-cardiotomy heart failure (HF), acute myocarditis, refractory fatal arrhythmia, and acute decompensation of chronic HF. Rescue with mechanical circulatory support remains the only means of survival in most of these patients. Over the past decade, an increasing number of assist devices have been developed for both temporary and long-term circulatory support. The extended indications, development of better support devices and management strategies, and improved results mandate all cardiology professionals to acquire knowledge of the currently available assist devices. Unfortunately, in Japan only a limited number of devices has been approved for clinical use and limited facilities have a ventricular assist system (VAS) program for long-term use. However, extracorporeal devices for acute HF are readily available for rapid implementation in the most facilities. These first-line devices for acute cardiogenic shock aim at stabilizing the patient’s general condition by providing enough systemic circulation and improvement of native heart function to enable eventual removal of the device. If recovery is unlikely, the patients can be transferred to a larger facility with a VAS program for longer term support aiming at either a bridge to transplantation or chronic assistance. Although the number of heart transplantations is severely limited, new modalities for long-term circulatory support, such as permanent therapy using continuous flow implantable VAS, is becoming a reality. Therefore, the short-term support to bridge the patient to these long-term therapies is becoming a more and more important strategy for the treatment of severe HF. Paracorporeal pulsatile devices still have an important role for patients requiring biventricular support or in the pediatric population. Chronic support aiming at heart transplantation using a paracorporeal device is an alternative option until the new rotary blood pumps become available in Japan. (Circ J 2009; Suppl A: A-42 – A-47)

Key Words: Cardiogenic shock; Extracorporeal life support; Heart failure; Mechanical circulatory assist; Venticular assists system

Extracorporeal Centrifugal Pump and Membrane Oxygenation

Extracorporeal life support (ECLS) using a centrifugal pump combined with extracorporeal membrane oxygenation (ECMO) is now considered an important tool for treating acute HF in all age groups, including neonates. In the setting of profound cardiogenic shock or cardiac arrest, ECLS is a viable option for resuscitation and initiating circulatory assist. When venous and arterial cannulas are inserted peripherally, the system is called percutaneous cardiopulmonary support (PCPS). Ready-made systems requiring only few minutes of priming time are commercially available. Various conditions causing cardiogenic shock are indicated for ECLS use. The Registry of Japanese society of PCPS reported the outcomes of PCPS for all indications from 2003 to 2005. Of 2,037 patients placed on PCPS, 60% were indicated for acute cardiopulmonary failure, 25% for post-cardiotomy HF, 10% for elective support for high-risk percutaneous coronary intervention or respiratory tract operation. Overall survival rate was approximately 50%.
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of death was cardiac failure in 65% and multi-organ failure in 11%. ECLS is for short-term use only because of the high rate of device-associated morbidity, including stroke, bleeding, infection, thromboembolic events and vascular complications that lead to limb ischemia or bleeding caused by vascular injury.11

The other important limitation of ECLS is inadequate left ventricular (LV) decompression and the increased LV afterload.11 Inotropic support is required to make the LV continue to eject and to prevent pulmonary hypertension. When LV decompression is poor, myocardial recovery is less likely and if VAS implantation is indicated afterward, an increased incidence of right ventricular (RV) failure results in high operative mortality.12 Therefore, patients with extremely poor LV function require a modality that can decompress the LV directly. Creation of a shunt through the atrial septum13 or direct suction with a LV or LA vent (Figure 1) has been reported for this purpose.14 Pagani et al described 7 patients who presented echocardiographic evidence of LA dilatation and pulmonary hypertension during ECLS use. They underwent the creation of an interatrial shunt and avoided severe lung hemorrhage.11

Because of the high rate of complications and limited mobility of the patients, switching to the longer duration of a VAS should be considered in patients who can not be weaned from ECLS in a few days to 1 week. There have been a number of reports describing that ECLS before VAS implant is a significant risk factor for mortality.12 However, the direct use of a VAS to salvage patients with cardiogenic shock and multi-organ failure is associated with a dismal outcome. Studies of emergency placement of long-term VAS in patients with profound cardiogenic shock and multi-organ failure report an operative mortality rate as high as >50%.15 Furthermore, the candidacy for long-term LVAS should be evaluated before its use. ECLS can provide reasonable circulatory support, permit recovery of end-organ failure and allow time to make further evaluation of pre-existing comorbidities, as well as recovery of end-organ and heart function aiming at subsequent therapies. This “bridge to bridge” strategy has been investigated extensively by Pagani et al11 at Michigan University. They used ECMO for 33 patients with refractory cardiogenic shock and severe hemodynamic instability: 75% of the patients were immediately post resuscitation from cardiac arrest or in cardiac arrest when ECMO was established. After a mean of 68h of ECMO support, 6 patients were weaned and 10 patients were bridged to an implantable LVAS. Among them, 40% of patients required RVAS. Overall, 36% of patients were discharged from hospital. Importantly, they could eliminate patients with irreversible brain damage or those contraindicated for heart transplantation from the implantable LVAS candidates, which are limited for bridge to heart transplantation.

The other way to effectively decompress the LV, prevent pulmonary hypertension, and then successfully bridge to a long-term assist device is application of biventricular support using direct cannulation into the great vessels and atrium as an open-chest procedure. The right and left atria are directly drained and both ventricles are unloaded. The difference from LVAS implantation is the elimination of graft anastomosis to the aorta and pulmonary artery, which may decrease the bleeding complications. Recently, at Minnesota University there has been application of CentriMag (Levitronix LLC, Waltham, MA, USA) through an open chest as biventricular support in 12 patients with refractory cardiogenic shock and multi-organ failure.16 Those patients were mostly resuscitated outside the hospital and neurological status was uncertain. Implantation of long-term support devices in this situation requires a long cardiopulmonary bypass time, a large amount of transfusion, and expensive devices, and its result has been reported as poor. In contrast, CentriMag provided good hemodynamic stability and recovery of end-organ function and there was time to confirm intact neurological status. Of the 12 patients, 8 were bridged to HeartMate LVAS as a bridge to transplantation. This “bridge to decision” strategy is useful for managing very sick patients and for saving costs.

New Percutaneous Devices for Acute HF

In critically ill patients with acute HF, open heart surgery using cardiopulmonary bypass often results in profound bleeding and multi-organ failure. Percutaneously utilized devices are less invasive, so are beneficial as a temporary bridge to more definitive therapy in many circumstances. Unlike the veno-arterial extracorporeal centrifugal pump (ECLS), which also can be quickly established, the new percutaneous devices directly decompress the LV. Therefore, superior unloading of the LV may lead to better functional recovery and may also prevent pulmonary hypertension and lung injury, resulting in a lower incidence of RV failure after LV support.
These percutaneous-type devices have become available in the United States and Europe. Impella Recovery (Abiomed, Inc, Danvers, MA, USA) is a percutaneously placed axial flow pump. The pump placed in the LV cavity actively drains blood into the ascending aorta. It requires exact placement of the pump in the LV and the inflow and outflow orifices in relation to the aortic valve (Figure 2A). The ideal application of this device is therefore acute cardiogenic shock because of acute myocardial infarction (AMI) requiring interventional procedures in the catheterization laboratory. It can be also used in combination with ECLS to decompress the LV. Seyfath et al conducted a randomized trial in 25 patients comparing intra-aortic balloon pump (IABP) and the Impella for cardiogenic shock caused by AMI and demonstrated superior hemodynamic support with the Impella, although the 30-day mortality rate was similar between the groups.

The TandemHeart System (CardiacAssist, Inc, Pittsburgh, PA, USA) is the other percutaneous system for supporting LV function. The tip of the inflow cannula is inserted peripherally and placed through the transatrial septum into the left atrium. Arterial return is achieved through a peripheral artery (Figure 2B). Burkhoff et al showed superior hemodynamic support by the Tandemheart compared with IABP in 42 cardiogenic shock patients randomized to either treatment, although the survival and adverse events were not significantly different. Idelchik et al used this device as a bridge to long-term LVAS implantation. All hemodynamic indices improved and systemic perfusion was reversed. After mean of 4.2 days of support, 14 of 18 patients successfully received long-term support devices or heart transplantation. None of their cases required right heart support at LVAS implant operation. Other device-related serious complications were less than in patients supported with ECLS. These devices could be, therefore, a better alternative to ECLS as a bridge to a long-term device in patients with profound cardiogenic shock and at high risk for immediate LVAS operation.

**Paracorporeal Pulsatile Devices**

Paracorporeal pulsatile devices are a pneumatically driven external assist device for uni- or biventricular support. The device is used as a bridge to recovery for post-cardiotomy HF or acute cardiogenic shock because of AMI or myocarditis. Longer term support as a bridge to transplantation is another option. Currently, 2 types of devices are available in Japan: Abiomed BVS-5000 (Abiomed Cardiovascular Inc, Danvers, MA, USA) and Toyo-Jo National Cardiovascular Center (NCVC) VAS (Nipro, Tokyo, Japan). The BVS-5000 is a vertical pump consisting of 2 individual chambers. Blood drains passively from the patient to the atrial chamber by gravity and the other ventricular chamber pneumatically drives blood into the outflow graft. The pump chamber has a capacity of 100 ml and can provide a maximum output of 5.5 L/min. Morgan et al have described 71 patients who underwent implantation of a BVS-5000, mainly for post-cardiomyopathy cardiogenic shock. The series included 19 cases as LVAS, 30 as RVAS and 22 as biventricular support. After a mean of 4.9 days of support, approximately 40% of patients were successfully weaned after myocardial recovery and 20% were bridged to either implantable long-term devices or heart transplantation. The BVS-5000 is a useful device for short-term support and has some advantages over ECLS on several points. The device provides pulsatile flow, which may have benefits for end-organ recovery, and increased mobility for the patient, who can be extubated and moved to a chair. The limitation is the requirement of relatively strong anticoagulation, and limited mobility compared with an implantable device. Therefore, in Japan its use is limited to a short-term bridge to recovery.

The Toyo-Jo NCVC VAS is a paracorporeal, pneumatic, diaphragm-type VAS. The pumps are made of Toyo-Jo TMS series segmented polyether polyurethane without a seam. The effective stroke volume is 70 ml and the maximum output in a mock system is 7.0 L/min. The external pneumatic drive console provides alternating positive and negative air pressure, which empties and fills the pump. Pumping rate and duration of the systolic and diastolic phases (% systole) can be set to make the pump fill and eject completely, so that stasis in the pump is prevented. The first clinical application of this device was in 1982 at the NCVC for a patient with post-cardiomyopathy shock. Although the device was originally designed only for acute HF, the lack of avail-
able LVAS for long-term use in Japan forced us to initiate use of the Toyobo device as a bridge for chronic HF aiming at heart transplantation. In 1992, we performed the first application in a patient with dilated cardiomyopathy. He was transported from Japan to the United States by air and bridged to transplantation after 119 days of support. Since then, the Toyobo LVAS has been the main device for the bridge to transplantation. We have had no other alternatives for long-term support in the majority of patients.

The Osaka University experience of the Toyobo-NCVC VAS consists of 68 patients who underwent implantation from January 1992 to June 2008. Mean age was 39.2±16.7 years (range 7–69). Etiologies of HF were idiopathic dilated cardiomyopathy in 38, ischemic cardiomyopathy in 16, myocarditis in 7, secondary cardiomyopathy in 5, and other in 2. Preoperatively, intubation was required in 46 patients (67.6%), IABP in 40 (58.8%), and ECMO in 32 (47.1%). Biventricular support was required in 20 patients (29.4%), among whom right heart support was removed in 8 and chronic right heart support with Toyobo device was performed in 5. The other 7 patients died from multi-organ failure while under support by RVAS early after the operation. Multivariate analysis demonstrated preoperative ECMO support and preoperative serum creatinine level were independent risk factors for requiring mechanical right heart support. As major device-related complications, cerebral hemorrhage occurred in 17 patients (25%), cerebral infarction in 20 (29.4%), mediastinitis in 10 (14.7%), and inflow/outflow cannula exit site infection in 19 patients (27.9%). Five patients underwent heart transplantation and 11 were weaned from LVAS, 9 under on-going VAS support and 43 have died while on VAS. Among the 11 patients who underwent LVAS weaning, 4 have been free of re-implantation of LVAS or heart transplantation. The mean duration of LVAS support was 224±283 days. Actuarial survival rate was 52.2% at 6 months and 36.3% at 1 year. Actuarial survival rate of the patients operated on in the past 5 years was 66.3% at 6 months and 45.9% at 1 year (Figure 3); 22 patients (36.1%) were supported for more than 6 months and 13 patients (21.3%) for more than 1 year. Early period (before 2002) and requirement of right heart support were the independent risk factors for patient survival by multivariate analysis.

The system of the Toyobo-NCVC device is similar to that of the other paracorporeal LVAS, such as Thoratec LVAS (Pleasanton, CA, USA) and Excor LVAS (Berlin Heart AG, Berlin, Germany) developed and used in the United States and Europe, respectively. The Toyobo LVAS experiences in comparison with their results are characterized by longer duration of support and a lower rate of successful bridge to heart transplantation. Serious shortage of donor organs could be the main cause of the difference. Secondly, the requirement for preoperative mechanical support and the presence of other organ dysfunction were higher in our series, which could be the main cause of the early mortality. Preoperative patient condition is a critical issue and earlier application is the key to success. ECMO support was required preoperatively in 47% of the patients. As shown by risk analysis for biventricular support, preoperative ECMO and renal dysfunction significantly correlated with the requirement for postoperative right heart support. These results are compatible with those from previous reports.

Our finding was also compatible with that of Dang et al who reported a higher mortality and lower bridge-to-transplantation rate in patients who required right HF.

On the other hand, an advantage of the paracorporeal devices is the ability of biventricular support. Tsukui et al recently reported excellent outcomes with biventricular VAS for morbid congestive HF. In their report, overall survival was 69%, and approximately 50% of the recent patients could be discharged from hospital with biventricular VAS. However, their patients underwent transplantation on average 86 days after the VAS operation. Long-term management with biventricular VAS is problematic because of the higher frequency of embolic events, not only in the systemic circulation but also in the pulmonary system.

Although the rate of device-related morbidity is significant and quality of life (QOL) is limited, the Toyobo LVAS can improve survival and provide durable support for longer than that of other paracorporeal LVAS used in other countries. Recently, a portable driver, the Mobart NCVC (Nipro, Tokyo, Japan), was developed. It gives patients more mobility and better QOL. Hospital discharge may become possible with the portable driver, as with the
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also as elective support after the operation. Ungerleider et

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Figure 4. Mobart-National Cardiovascular Center portable driver for
the Toyobo-National Cardiovascular Center ventricular assist device
shown in Figure 3.

Thoratec LVAS. Paracorporeal devices will still play an
important role in supporting biventricular failure patients
or potentially recoverable candidates.

Pediatric Circulatory Support

Mechanical circulatory support is an important tool for
children with refractory HF. There are many limitations in
relation to the inherent properties of children: small body
size, and immature immune and coagulation system. Improve-
ments of current systems and management strategies, and
innovation of new devices suitable for small children are
under intense investigation.

Two forms of assist are currently available: ECMO and
paracorporeal VAS. ECMO is the most common form of
mechanical support and is the best option for acute decomp-
ensation. It provides not only biventricular assist but also
respiratory support by supplying oxygenated flow. There-
fore, it can be used in a variety of settings to provide support
to critically ill children. Special considerations are required
for their individual anatomy (uni- or bi-ventricular, shunt,
etc), physiology (cardiac or respiratory function, pulmo-
nary hypertension, etc), cannulation and management. As
experience has grown, new types of application have
evolved. Functional univentricular circulation was not often
indicated for ECMO previously. However, recent improve-
ments in the results have extended its application not only
for inability to separate from cardiopulmonary bypass, low
cardiac output, cardiac arrest, and thrombosed shunt, but
also as elective support after the operation. Ungerleider et

regenerative therapies may be important to achieve this goal.

Future Perspectives

In the last few years a rapid shift from pulsatile to rotary
blood pumps has occurred as the choice for long-term assist
circulation. Continuous flow rotary pumps have many
advantages, including a small pump size, elimination of
reservoir and valves, and long-term durability, which also
give the patient better QOL. Many types of rotary pumps
have become available and are now used as the first-line
device for long-term support. Lack of biventricular support
and pediatric application are the disadvantages of the rotary
pumps, but those are under intense investigation and will
become available in the near future. In such circumstances,
the use of extracorporeal or paracorporeal devices will be
limited to acute cardiogenic shock. Those devices are used
to temporarily stabilize the patient’s condition as a bridge
to further therapy, including heart recovery, long-term device
implantation or heart transplantation. Less invasiveness
will be the most important point for future extracorporeal
device design and application. Anti-thrombogenicity, easy
applicability and portability will also be important factors.
Those improvements may also expand the utilization of
those devices as a portable rescue tool for HF. The use of
LVAS as a bridge to recovery for chronic HF is also attrac-
tive. Strategies for multidisciplinary treatment combining
VAS with other modalities, such as myocardial regenera-

developmental outcomes were reported.

Although ECMO is the main device used for children
requiring mechanical support, its use is limited to short-term
support. Long-term use is associated with significant risks,
including infection, thromboembolism, bleeding, and pro-
hibition of mobility of patients. VAS implantation is the
treatment of choice for children requiring long-term support
as a bridge to transplantation or to recovery. Unlike the many
selections for adult patients, there are only limited options
available for children. The use of pneumatic paracorpo-
real pulsatile devices is, however, increasing. The VAS,
EXCOR Pediatric (Berlin Heart AG, Berlin, Germany),
has specially been developed for use in children, toddlers
and even babies. This has become possible because of the
5 different sizes of blood pumps (10–60 ml volume) and the
wide range of cannulas. There are tri-leaflet polyurethane
valves at the inflow and outflow sockets. The EXCOR has
the largest number of pediatric applications of a VAS.
Approximately 300 children worldwide have been sup-
ported with the EXCOR. A greater percentage of patients
require biventricular support compared with the adult popu-
lation, but success rates of 51–78% of bridging to transplant
have been reported.

In Japan, only the Toyobo-NCVC in adult size is cur-
rently available. Experience is limited and only approxi-
mately 25 cases under the age of 15 have undergone LVAS
implantation (personal communication). Concerns about
the use of oversized devices have been raised. Large stroke
volume causes systemic hypertension and subsequent intra-
cranial hemorrhage, and stasis in the device can be related
to thromboembolic complications. New devices specialized
for use in small children are required. In the United States,
funds for development of pediatric VAS (mainly rotary
pumps) have been awarded by the National Heart, Lung
and Blood Institute and it is hoped that several devices
will become available in the near future.
References


