Mechanical circulatory support (MCS) devices are changing heart failure therapy. A spectrum of devices have become essential to the management of a variety of heart failure scenarios and, in the next few decades, this spectrum will expand and improve thousands of lives each year. The field has grown slowly and at considerable cost over the past 50 years but is now moving rapidly. Devices as small as a pencil and up to the size of two fists are being implanted in record numbers, with a total of over 15,000 implants worldwide. Many devices have been retired, some replaced by smaller, more efficient pumps and some eliminated by costly regulatory requirements and market forces. Several new devices are undergoing animal and early human trials but the field has been reduced to:

• one left ventricular assist device (LVAD), approved for long-term use;
• several LVADs approved for short-term use as a bridge to transplantation or recovery;
• one total artificial heart (TAH), approved for use as a bridge to transplantation; and
• several temporary rescue pumps, which could be used to support either ventricle or as an extracorporeal membrane oxygenation (ECMO) system to support the heart and lungs.

This technology brings surgeons, cardiologists, engineers, nurses, and administrators together in a powerful consortium that challenges industry and government to make devices more affordable and more readily available. Undoubtedly, there will be a greater use of these devices in short-term crises, in the long-term treatment of chronic heart failure, for use as a bridge to transplantation and for the recovery of native hearts. Outpatient care of people using MCS devices enables communication between referring physicians and local communities but creates a need for the dissemination of general knowledge on the devices and the care and management of patients using these devices.

Cost is a major consideration. Most long-term devices cost about US$75,000 per artificial ventricle. Temporary devices are cheaper, ranging from about US$10,000 for the simplest to US$25,000 per ventricle for the more complex. At US$2,000–5,000 per day for acute hospital care, length of hospital stay rapidly becomes the limiting factor. Reduction in the cost of MCS has been envisioned as an intermediate goal of the pioneers in the field. It was hoped that the general acceptance of MCS devices—and their more widespread use, which could in turn improve manufacturing efficiency—would reduce cost. As of mid-2010 however, pump cost has not decreased despite an increase in the number of devices sold. Meanwhile, daily hospital stay cost has increased and prolonged hospitalizations are often necessary for very sick patients. An ideal MCS device should:

• be easy to implant;
• provide blood flow and perfusion adequate to support the patient and resuscitate the organs;
• have a low complication rate;
• be easy to explant;
• be durable for the intended length of implantation; and
• be documented as successful by at least one multi-institutional study.

Abstract
Mechanical circulatory support devices have been in development since the late 1950s and are now challenging cardiac transplantation as the primary intervention for end-stage congestive heart failure. A diverse selection of devices is currently available, ranging from the size of a pencil to the size of two fists and with a spectrum of pumping characteristics, flows, positions in the chest, risks, and complications. The two basic types of device are pulsatile ‘volume displacement’ pneumatic pumps and non-pulsatile ‘rotary’ electric pumps. Over 15,000 patients have undergone device implantation. The majority of patients are discharged and results are accumulating that will allow us to determine when in the progression of heart failure we should add mechanical circulatory support devices to patient therapy. Selection criteria are evolving from risk factor analyses conducted over the past decade. A national registry will help to both organize patient and device selection and catalogue complications and long-term results.

Keywords
Left ventricular assist device (LVAD), total artificial heart (TAH), pulsatile flow, continuous flow, multivariate analysis, registry

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Mechanical Circulatory Support in Heart Failure
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Multivariate analyses\textsuperscript{1,2} have begun to help us understand the reasonable indications and contraindications for the use of these pumps. Risk factors for LVAD implantation include:

- right ventricular failure;
- renal failure;
- thrombocytopenia;
- elevated international normalized ratio (INR);
- elevated total bilirubin level; and
- previous cardiac operation.

These are additive: thus, in the Lietz system,\textsuperscript{3} a score of >20 is associated with a one-year survival rate of 30%, while lower scores are associated with a higher survival rate. In a multicenter trial of the TAH\textsuperscript{4} that looked at 43 risk factors, none of those found for LVADs were predictive of poor outcome, suggesting that the TAH could be used in sicker patients without a significant increase in risk. Even so, contraindications to TAH use include:

- severe malnutrition;
- inability to reverse the disease state to potential heart recipient status;
- chronic end-stage organ failure (renal, hepatic, lung); and
- small cardiac size.

Indications for LVAD\textsuperscript{5} and TAH\textsuperscript{6} implantation have followed the tenet that sicker patients, such as those with irreversible biventricular failure, should receive a TAH, while less sick patients, such as those with reasonable function of the right ventricle, are LVAD candidates. As smaller devices with lower flows are developed, new sets of indications and contraindications will evolve.

**Types of Pump**

Mechanisms of pumping are referred to as ‘volume displacement’ or ‘rotary’. A volume displacement pump, like the heart, is pulsatile. It has inflow and outflow valves and a diaphragm that exerts pressure on blood, creating a pulse. Volume displacement pumps typically have a stroke volume of 50–70ml and deliver a physiologic pulse pressure. The output of the device depends upon the amount of filling or preload and that the device is not afterload-limited. It will pump against any resistance or pressure in the systemic or pulmonary circulation. In vivo, the volume displacement-type TAH delivers 7–9l/minute at a central venous pressure (CVP) of 8–15mmHg. In pneumatically driven TAHs, balancing the flows of the two ventricles is not a problem.

Extracorporeal pulsatile pumps can be used as univentricular support systems to support either the left or right ventricle. They are also used as implantable pumps, with only a transcutaneous driveline, or as extracorporeal pumps, connected by transcutaneous tubes to the heart. Problems with such applications include the size and length of the inflow and outflow cannulas: these place physical limitations on the amount of flow that is generated. Typically, they flow at 4–6l/minute under optimal conditions. Two types of rotary blood pump exist—axial flow and centrifugal—both of which produce a continuous, non-pulsatile flow. Both use rapidly spinning rotors to create blood flow. Axial flow pumps have one moving part, with blades or vanes, which rotates within a tubular structure at speeds of 8–10,000 revolutions per minute (RPM), resembling a turbine or jet engine. Centrifugal pumps are circular and either flat or cone-shaped: blood is ejected from the peripheral part of the device where the flow is maximal. These are usually run at approximately 2,000RPM. Centrifugal pumps have been used by some cardiac surgery teams for routine cardiopulmonary bypass for many years.

There are no valves and, in the case of LVADs, when the device is off, blood can flow backwards, creating the equivalent of acute aortic regurgitation. Moreover, on the inflow side (where blood enters the pump), these devices develop negative pressure that can cause ventricular collapse. On the outflow side, these devices are afterload-sensitive and lose efficiency against mean arterial pressures >90mmHg. Typically, rotary pumps generate some pulsatility: this arises from the left ventricle pumping through the device. Depending on the filling of the left ventricle, it may have enough contractility to open the aortic valve. As the RPM increases to the point that the left ventricle is relatively empty, the pulsatility from the native ventricle disappears. In this situation, the patient has no palpable pulse and measurement of the mean arterial pressure must be performed with a blood pressure cuff and Doppler ultrasound.

**Flow**

Flow of blood is life-saving and the basic premise of every MCS device is to increase blood flow. As seen in Table \ref{table:flows}, a wide range of flows exist. The design of a device determines flow. Smaller devices that are percutaneous,
or easier to implant, have lower flows. At flows below 4 l/minute, devices assist cardiac output from the native heart; above 4 l/minute, devices tend to replace the function of the native heart.

In patients, a cardiac index of <2 l/minute/m² is generally regarded as ‘cardiogenic shock’. With the implantation of a MCS device, the aim is to improve the cardiac index to 2.5–3 l/minute/m². The goal of the implant might be to assist the circulation, or it might be to take over the circulation and have sufficient output to keep the patient alive, resuscitating any failing organs and returning the patient to reasonable function, including normal activity, normal nutrition and a good quality of life. The patient should be in better health than he or she was before the implant and free of complications. The flow volume generated by the pumps is limited in the case of LVADs by the blood flow from the right side of the heart to the left. Right ventricular function is a major determinant of LVAD output. The size and length of the inflow tube or cannula, as well as the outflow cannula, create resistances that may be flow-limiting. In Figure 4, the inflow diameter and length are shown, as are the length of the flow pathway through the heart and the length of the outflow cannula. The TAH has the shortest pathway, approximately the same as the normal human heart.

### Table 1: Comparison of Flows Obtained with Mechanical Circulatory Support Devices

| Device                  | Inflow Diameter (mm) | Right Ventricle Dependence | Afterload Dependence | Outflow Diameter (mm) | Flow (l/minute) |
|-------------------------|-----------------------|----------------------------|----------------------|------------------------|-----------------|
| Impella®                | 2.7                   | Yes                        | Yes                  | 2.7                    | 2.5             |
| TandemHeart®            | 6                     | Yes if LVAD, No if BiVAD   | Yes                  | 6                      | 5               |
| HeartMate II®           | 19                    | Yes                        | Yes                  | 14                     | 4–6             |
| Syncardia Total Artificial Heart | 27                   | No                         | No                   | 25                     | 7–9             |

### Figure 3: Comparing the Left Ventricular Assist Device with the Total Artificial Heart

### Figure 4: Inflow Diameter and Cannula Length are Determinants of Resistance and Flow Capacity of Devices

| Device             | Inflow diameter (mm) | Distance blood travels for single ventricle (cm) | Inflow | Device | Outflow |
|--------------------|----------------------|--------------------------------------------------|--------|--------|---------|
| Thoratec (Atrial)  | 10                   |                                                  |        |        |         |
| Thoratec (Apical)  | 13                   |                                                  |        |        |         |
| Heartmate II       | 19                   |                                                  |        |        |         |
| Heartware          | 14                   |                                                  |        |        |         |
| Cardiowest         | 27                   |                                                  |        |        |         |
Heart Failure

The capability of an MCS device to create blood flow is dependent on the right ventricle. LVADs, as seen in Figure 3, depend upon flow from the right side of the heart. This, in turn, is dependent on right ventricular function and pulmonary vascular resistance. Because of these factors, it is rare to see cardiac outputs of >6l/minute in patients following LVAD implantation. In cases of significant right heart failure, a right ventricle assist device (RVAD) is necessary to sustain the patient at least temporarily. This situation increases mortality by approximately 50%. Ventricular arrhythmias can also cause right ventricular failure and result in significant drops in LVAD output. In order to decrease this risk, recent studies have eliminated patients from LVAD implantation if they have right heart failure.

The TAH is not dependent upon the native right ventricle or the pulmonary vascular resistance. If an adequate filling pressure of 10–15mmHg is present, the TAH will pump at >7l/minute immediately after implantation.

While it might seem plausible that the output generation of biventricular assist devices (BiVADs) would be similar to the TAH, this has proven not to be the case. Our experience suggests that, with BiVADs, the best outputs are in the 5l/minute range. Often this is at fairly elevated CVP. Our impression has been that this is related to the resistance in the long, narrow inflow cannulas on both the right side and the left side. The problem is worse on the right, because cannula positioning is more difficult. The consequences of higher filling pressure could be worse here than on the left side, the most significant being decreased renal perfusion resulting from high CVP.

What is an Adequate Cardiac Output with Device Support?

Most authors agree that a cardiac index of ≤2l/minute/m² is cardiogenic shock. Our multivariate analysis of risk factors for the survival of patients in our program receiving MCS found that patients survived if their cardiac index could be raised to 2.5l/minute/m². For these patients—in whom clotting and inflammatory systems are activated and, in most cases at least one organ is beginning to fail—it seems prudent to provide more than the minimal cardiac index. We aim to raise the cardiac index to 2.5–3.5l/minute/m². This means that in many Americans—with body surface areas of 1.9m² for females and 2.1m² for males—an index of 3l/minute/m² will require an output of 6l/minute. Based on this, we have used extracorporeal BiVADs for patients with body surface areas of <1.7m² unless they have a very large end-diastolic diameter of the left ventricle (>0.7cm), as visualized by echocardiography. For larger patients and those with very large native ventricles even though their body size is small, we have used the TAH, because it provides high flows and gives the patient a greater margin of safety. Patients who are more stable and do not have clinical right heart failure are treated with LVADs.

Increasing flow is the key to resuscitation but devices must also reduce CVP. Typically, sicker patients have a CVP >25mmHg. If, simultaneously, the pulmonary artery pressure is high—in the 50–70mmHg systolic range—it is likely that a substantial drop in left ventricle filling pressure will lead to reduced pulmonary artery pressure and a reduction in CVP. In sicker patients with pulmonary edema, or with lower pulmonary artery pressures but high CVPs, it is unlikely that the CVP will be reduced by an LVAD; biventricular support should, therefore, be initiated from the start.

Adverse Events

Each approved device and the risks and benefits associated with their use have been subject to tight scrutiny in a study supervised by the US Food and Drug Administration. The major adverse events resulting from MCS are related to coagulation, anticoagulation, infection and inadequate flow (due to poor device/patient selection, right heart failure, and/or mechanical problems).

Immediately after implantation, central nervous system damage could result from air or particulate embolism, or from reduced cerebral blood flow. Later, strokes can result, either from emboli caused by the pump or from spontaneous intracerebral bleeding. The currently approved devices have stroke rates of 10%. most of these strokes are associated with device implantation, although some occur spontaneously during device support. Anticoagulation methods vary among devices, depending upon the intrinsic device coagulability. Some devices, such as the HeartMate II LVAD (Thoratec Corporation, California), cause an anticoagulant effect that permits no or minimal anticoagulation. Others, such as the SynCardia Total Artificial Heart (SynCardia Systems, Inc., Arizona), cause hypercoagulability that must be controlled with anticoagulation and antiplatelet therapy.

Scenarios for Device Implantation

Acute or Emergent Decompensation

This is perhaps the most common scenario and has the highest mortality rate. In any patient who is judged as eligible for resuscitation but fails 15–20 minutes of chest compression and advanced cardiovascular life support, prompt implantation of a blood pump could save a life. Placement of cannulas on an emergent basis for ECMO, using the percutaneous technique or using femoral venous cutdown, is the easiest and most readily available technique. Minimally invasive pumps, that decompress the left ventricle, are very helpful. If available, the Impella 2.5 heart pump, manufactured by Abiomed, Massachusetts (transarterial passage, retrograde across the aortic valve into the left ventricle, providing 2.5l/minute flow), or the TandemHeart®, manufactured by CardiacAssist, Inc., Pennsylvania (a percutaneous trans-septal catheter draining the left atrium, while a centrifugal pump delivers flow to the femoral artery, providing 4–5l/minute flow), are preferable to ECMO. In hospitals with experience using these techniques, 40–60% of cardiac arrest patients are salvaged. In centers where the time to MCS is more than hour, the salvage rate is <15%. In these situations, intra-aortic balloon pumping is helpful only if there is return of a cardiac rhythm and an effective left ventricular ejection. It would be contraindicated in an “arrested” patient where blood flow is the life-saving factor. Even in patients with a cardiac rhythm and left ventricle ejection, intra-aortic balloon pumping seldom adds more than 10% to the cardiac output and, in addition, can cause morbidity. We have reserved it for patients who are resuscitated and for whom ischemia is the etiology of their heart failure.

Once any temporary MCS pump is in use, it can be used as a bridge to a decision. All of these devices can be used for at least five days and some can be left implanted for up to two to three months if necessary.
Verification of neurologic, renal, hepatic, and hemostatic function can be performed during the period of observation, as well as cardiac evaluation via monitoring continuous cardiac output, pulmonary artery pressure and arterial pressure, and echocardiography. Primary use of a longer-term device is expensive and not indicated in most of these patients.

The INTERMACS® Patient Classification

The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS®) was formed approximately two years ago to serve as a national registry for all types of MCS device. As time passes and outcome data are recorded, this promises to be an excellent source of registry information. A new set of patient profiles is being developed to subdivide groups of patients who were formerly placed in the New York Heart Association (NYHA) Functional Classification categories IV and advanced III. These seven groups may be further subdivided as more data are accrued, especially in the ‘critical cardiogenic shock’ category. The list of profiles that follows aims to allow for consistent stratification of risk and could be used to identify groups of patients that may benefit from the various types of MCS device.

1. Critical cardiogenic shock.
2. Progressive decline.
3. Stable but inotrope dependent.
4. Recurrent advanced heart failure.
5. Exertion intolerant.
6. Exertion limited.
7. Advanced NYHA III.

Waiting until patients reach the crisis stages of decompensation may no longer be necessary. Implantation of smaller devices earlier in the progression of the disease is desirable but only when the combined risks of the implantation, projected over time, are fewer than those of continued medical therapy. This registry may also help define the very sickest patients. Some should have a short-term device to buy time—a bridge to a decision—before progressing to more expensive, riskier, and longer-term support; others should have continuing supportive therapy or hospice care.

Concluding Remarks

Controversy surrounds the application of what is regarded as a very expensive, technology-heavy approach to end-stage heart failure. Cardiac transplantation has been the accepted therapy for selected patients for over 25 years but the number of patients with heart failure has grown, yielding up to 100,000 patients per year in the US that could benefit from heart replacement. For the past 10 years, the maximal number of heart transplants performed in the US has been steady at about 2,200 per year. Given the improved quality of life for users of MCS devices and the option in most cases for outpatient care after several weeks, MCS devices may, in the very near future, displace cardiac transplantation as the mainstay for treating end-stage heart disease.

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