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AHA Scientific Statement

Recommendations for the Use of Mechanical Circulatory Support: Device Strategies and Patient Selection

A Scientific Statement From the American Heart Association

Jennifer L. Peura, MD, Chair; Monica Colvin-Adams, MD, MS, FAHA, Co-Chair; Gary S. Francis, MD, FAHA; Kathleen L. Grady, PhD, APN, FAHA; Timothy M. Hoffman, MD, FAHA; Mariell Jessup, MD, FAHA; Ranjit John, MD; Michael S. Kiernan, MD; Judith E. Mitchell, MD, FAHA; John B. O'Connell, MD; Francis D. Pagani, MD, PhD, FAHA; Michael Petty, PhD, RN; Pasala Ravichandran, MD; Joseph G. Rogers, MD; Marc J. Semigran, MD, FAHA; J. Matthew Toole, MD, FAHA; on behalf of the American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology, Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation, Council on Cardiovascular Disease in the Young, Council on Cardiovascular Nursing, Council on Cardiovascular Radiology and Intervention, and Council on Cardiovascular Surgery and Anesthesia

The era of mechanical circulatory support (MCS) began in 1953 with the development of cardiopulmonary bypass to facilitate open heart surgery.[1] In 1964, the National Heart Institute (now the National Heart, Lung, and Blood Institute) funded the Artificial Heart Program and became actively involved in MCS development. This led to requests for Proposals issued in 1977 and 1980, which laid the foundation for the development of implantable MCS for long-term use, including devices capable of hospital discharge, in the 1990s. Although heart transplantation is now commonplace at many hospitals, the inadequate supply of donor hearts and patient contraindications to transplantation continue to severely restrict its application. As the demand for long-term replacement of diseased hearts increases, there is a clear need for innovative, safe, and durable MCS to treat the growing population of patients with advanced heart failure (HF). Many exciting changes in the field of MCS have occurred in the past few years, including the development of smaller portable pumps and the concept of destination therapy (DT), or permanent pump placement as an alternative to heart transplantation. Currently, there are no published guidelines for the use of MCS. Thus, it is our intent that this statement will provide the contemporary cardiologist and other HF providers with an understanding of general considerations when determining the appropriateness of MCS.

Definition of Advanced HF

There is little hope that complete consensus will ever be reached on the definition of advanced HF, but most physicians caring for such patients on a regular basis readily identify the characteristics of these patients. Advanced HF patients are those with clinically significant circulatory compromise who require special care, including consideration for heart transplantation, continuous intravenous inotropic therapy, MCS, or hospice.[2,3] Typically, such patients have symptoms at rest or with minimal exertion and cannot perform many activities of daily living.[3] Commonly used objective measures of functional limitations include a peak $V\dot{o}_2 \leq 14$

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$mL \cdot kg^{-1} \cdot min^{-1}$ (or <50% of expected) and a 6-minute walk distance <300 m.[3] Many have cardiac cachexia, are failing or intolerant of conventional HF therapy, and require repeated hospitalization for more intensive management.[4] Advanced HF patients usually have a life expectancy of <2 years without heart transplantation or MCS, and ≈50 000 patients each year in the United States die of advanced HF.[4]

Options for Advanced HF

When a patient presents with advanced HF, a candid discussion of prognosis is appropriate. In addition to a review of advanced therapies such as transplantation and MCS, the benefits of and drawbacks to resuscitation and deactivation of defibrillators and the choice of a family spokesperson or surrogate should be addressed with the patient and the patient's family. On occasion, outpatient intravenous inotropic agents are prescribed, but these drugs are strictly palliative and can foreshorten life.[5,6] Palliative inotropic therapy should be reserved for only those patients who have a reproducible and marked improvement in symptoms with inotropic therapy. Hospice has traditionally been reserved for patients with a life expectancy of ≤6 months, but this operational policy may be difficult in the setting of advanced HF because healthcare providers cannot accurately predict the end of life in such patients. Policies are being revised to allow patients with HF to benefit from hospice services.

Heart transplantation remains the definitive therapy for advanced and refractory HF. However, heart transplantation remains challenged by inadequate donor supply, finite graft survival, and long-term complications of immunosuppressive therapy. Thus, there is a need for more refined and durable MCS options. The recent development of smaller, more durable, and safer ventricular assist devices (VADs) has enabled MCS to emerge as a practical and effective form of therapy, either until heart transplantation can be performed (as bridge to transplantation [BTT]) or increasingly as an alternative to transplantation as DT.

As the MCS field evolves, practitioners caring for advanced HF patients will require an understanding of the appropriate application of MCS. In addition, an increasing number of community programs seek to provide alternative therapy for HF. As MCS use and management move beyond the purview of academic transplant centers, it is essential that the indications for MCS and the essentials of device management are broadly understood. Although we have provided a summary of current professional society guidelines in Table 1, it could be argued that the expanding use of MCS is not reflected in current guideline statements.[7–11] Accordingly, in this statement, we provide recommendations based on currently available data and the consensus of leaders in the field of MCS.

Management Strategies for the MCS Patient

Selection Criteria and Decision Process

The approach to MCS is determined by the trajectory of HF progression and overall clinical status. Because there are temporary and durable device options, extracorporeal, implantable, or percutaneous strategies for MCS are as broad and variable as the patients requiring this therapy. MCS may be used as a BTT for transplantation-eligible patients and as DT for those who are transplantation ineligible. These designations are fluid, however, because the patient's candidacy for either therapy may change over time (Figure 1). For example, a DT patient may become transplant eligible after significant improvement in comorbidities that previously precluded consideration for transplantation. Alternatively, a transplantation-eligible patient may become ineligible after MCS because of perioperative complications, progression of comorbidities, or personal preference. In circumstances when a patient presents in cardiogenic shock, it may not be possible to fully determine candidacy for transplantation. MCS may be used to determine neurological recovery and to stabilize potentially reversible comorbidities. In these situations, MCS is used as a bridge to decision or bridge to recovery.

It is important to underscore 2 important principles that have evolved over the past decade. First, some patients are

Table 1. Current Recommendations for MCS

ACCF/AHA 2009 HF guidelines[7]
Consideration of an LVAD as permanent or destination therapy is reasonable in highly selected patients with refractory end-stage HF and an estimated 1-year mortality >50% with medical therapy (*Class II; Level of Evidence B*)
HFSA comprehensive HF practice guidelines[8]
Patients awaiting heart transplantation who have become refractory to all means of medical circulatory support should be considered for an MCS device as a BTT (*Level of Evidence B*)
Permanent mechanical assistance with an implantable LVAD may be considered in highly selected patients with severe HF refractory to conventional therapy who are not candidates for heart transplantation, particularly those who cannot be weaned from intravenous inotropic support at an experienced HF center (*Level of Evidence B*)
Patients with refractory HF and hemodynamic instability and/or compromised end-organ function with relative contraindications to cardiac transplantation or permanent MCS expected to improve with time or restoration of an improved hemodynamic profile should be considered for urgent MCS as a bridge to decision; these patients should be referred to a center with expertise in the management of patients with advanced HF (*Level of Evidence C*)
Canadian HF guidelines[9]
MCS may be offered to selected individuals with end-stage heart failure who are inotrope dependent and do not meet the traditional criteria for cardiac transplantation (*Class IIb; Level of Evidence B*)
ESC guidelines 2008/2010[10,11]
Current indications for LVADs and artificial hearts include bridging to transplantation and managing patients with acute, severe myocarditis (*Class IIa; Level of Evidence C*)
Although experience is limited, these devices may be considered for long-term use when no definitive procedure is planned (*Class IIb; Level of Evidence C*)
LVAD may be considered as destination treatment to reduce mortality (*Class IIa; Level of Evidence B*)

MCS indicates mechanical circulatory support; AHA, American Heart Association; ACCF, American College of Cardiology Foundation; HF, heart failure; LVAD, left ventricular assist device; HFSA, Heart Failure Society of America; BTT, bridge to transplantation; and ESC, European Society of Cardiology.

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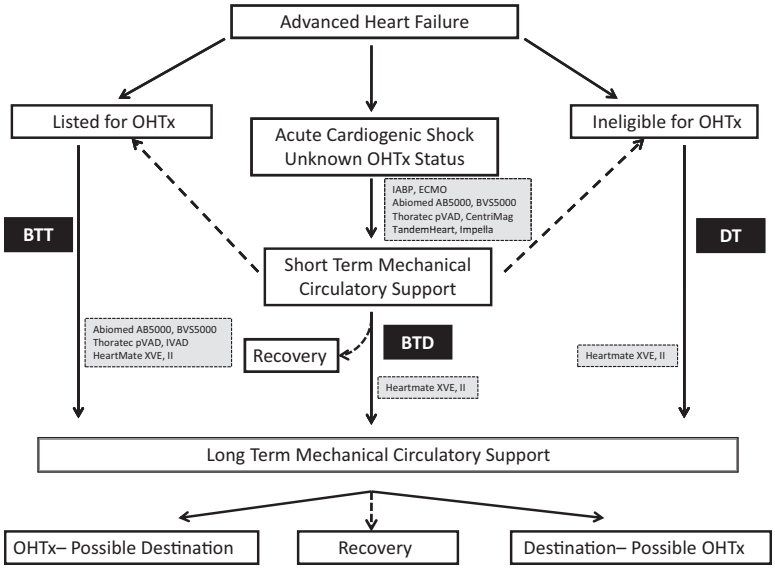

Figure 1. Device selection flow chart. OHTx indicates orthotopic heart transplantation; IABP, intra-aortic balloon pump; ECMO, extracorporeal membrane oxygenation; pVAD, Paracorporeal Ventricular Assist Device; BTT, bridge to transplantation; DT, destination therapy; and BTD, bridge to decision.

too profoundly ill with multisystem organ failure to benefit from the very best of MCS and aggressive inotropic therapy. Second, complex decisions about candidacy for transplantation or MCS are best made by an experienced, multidisciplinary team. Although it may become appropriate for smaller programs to implant elective DT MCS in highly selected patients, more acutely ill patients should be referred to quaternary care hospitals that are accustomed to the management of such patients. In the following sections, strategies for MCS are discussed.

Indications for MCS

Bridge to Recovery

The first application of extracorporeal MCS focused on temporary maintenance of the circulation after an acute event until the occurrence of cardiac recovery. The earliest clinical example was the use of MCS in patients with postcardiotomy shock in whom failure to wean from cardiopulmonary bypass was considered certain death unless the patient could be rescued with temporary MCS. This pattern established the concept and indication of bridge to recovery in which temporary MCS sustained the circulation until cardiac recovery. A robust experience with temporary MCS for failure to wean from bypass led to the application of MCS in nonpostcardiotomy settings such as cardiogenic shock caused by myocardial infarction, fulminant or acute myocarditis, or acute cardiac allograft dysfunction after heart transplantation.

Compared with early options for MCS, modern devices (Table 2) provide longer duration and more versatile support. These devices, called nondurable MCS, may be used as a first step when rapid support is necessary in patients with cardiogenic shock who are at too high a risk for implantation of a durable device or as an alternative to durable implantable devices if recovery is possible. For these patients, a bridge with a nondurable device provides essential stabilization and permits clarification and potential reversal of the other medical issues that may interfere with a satisfactory outcome after transplantation or long-term device placement. The following nondurable devices are used for bridge to recovery and for temporary support until more definitive therapies can be used in patients in whom myocardial recovery does not occur.

Intra-Aortic Balloon Pump

The intra-aortic balloon pump (IABP) is broadly used and is commonly the first step in the treatment of cardiogenic shock. The IABP provides hemodynamic support for cardiogenic shock by diastolic augmentation of aortic pressure and left

Table 2. Devices Available for Short-Term MCS

Device	Manufacturer	Mechanism	Position	Duration
IABP	Multiple	Counterpulsation	NA	Days
ECMO	Multiple	CPB	NA	Days–weeks
BVS5000, AB5000	ABIOMED	Pulsatile	R, L, or Bilateral	Weeks
Thoratec pVAD	Thoratec	Pulsatile	R, L, or Bilateral	Weeks
CentriMag	Levitronix	Centrifugal	R, L, or Bilateral	Weeks
TandemHeart	CardiacAssist	Centrifugal	pMCS	Days
Impella	ABIOMED	Axial flow	pMCS	Days

MCS indicates mechanical circulatory support; IABP, intra-aortic balloon pump; NA, not applicable; ECMO, extracorporeal membrane oxygenation; CPB, cardiopulmonary bypass; R, right; L, left; pVAD, percutaneous ventricular assist device; and pMCS, percutaneous mechanical circulatory support.

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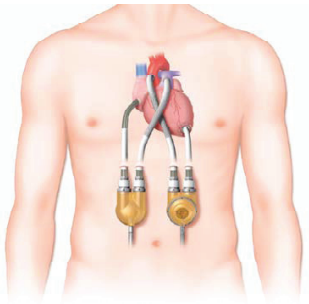

Extracorporeal pulsatile
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Implantable continuous flow
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Implantable pulsatile
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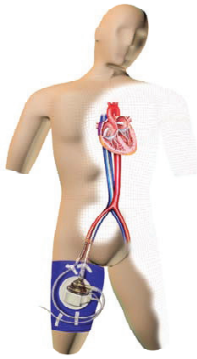

Percutaneous
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Figure 2. Device diagrams. Reprinted with permission from Thoratec and from CardiacAssist.

ventricular afterload reduction. Coronary perfusion is also increased, which may be important in the setting of increased ventricular diastolic pressure, even in the absence of critical coronary artery stenosis. Although relatively easy to insert in the community setting, the use of the IABP is limited to short durations of support because of potential arterial complications and the inability to mobilize patients. It may be insufficient in the setting of marked cardiac failure.

Extracorporeal Membrane Oxygenation

Extracorporeal membrane oxygenation (ECMO) is used to treat medically refractory cardiogenic shock when there is poor oxygenation, and ECMO can be a rapid option for emergency biventricular support. ECMO uses a nonpulsatile pump, membrane oxygenator, and inflow and outflow cannulas. Arterial and venous access can be obtained via peripheral cannulation of the femoral vessels, which can be applied rapidly at the bedside.[12] Survival of patients treated with ECMO reflects the critical nature of the patients in whom it is used. In adults, 1 study reported 58% survival to hospital discharge,[13] and another reported survival rates of 76% (3 days), 38% (30 days), and 24% (5 years).[14] In the pediatric population, ECMO use is more prevalent,[12] yet survival is still modest (43%–54%).[15,16] Outcomes may be improved when ECMO is used for specific indications such as acute myocarditis, in which survival was reported to be as high as 83% in pediatric[17] and 75% in adult[18] patients. Major limitations for the use of ECMO remain its lack of durability (weeks of support), limited availability, necessary perfusion support, and complications related to vascular access.

Extracorporeal MCS

Early pulsatile, extracorporeal devices provided salvage support for patients in cardiogenic shock who otherwise faced an extremely high risk of mortality.[19] These extracorporeal devices were implanted via a traditional sternotomy with an external pumping chamber and drive console (Figure 2). The first of these devices was the Abiomed BVS5000 (ABIOMED, Inc, Danvers, MA), a nondurable, extracorporeal, pulsatile, pneumatic device with a large external controller. It was approved by the US Food and Drug Administration (FDA) after a prospective, nonrandomized, multicenter trial of 55 patients with postcardiotomy shock. Fifty-five percent of patients were weaned from support, and 29% of patients survived to discharge.[20] The following pulsatile pumps have been approved for rescue therapy: Abiomed AB5000 (ABIOMED, Inc) and the Thoratec Paracorporeal Ventricular Assist Device II (Thoratec Corp, Pleasanton, CA). Survival with the Paracorporeal Ventricular Assist Device was 48% in a nonrandomized trial of 29 patients with postcardiotomy shock.[21–23] Finally, the CentriMag (Levitronix LLC, Waltham, MA) is a nondurable, extracorporeal, continuous, centrifugal-flow pump with a magnetically levitated rotor and external controller that is designed to support the left, right, or both ventricles.[24,25] This system is capable generating flows up to 10 L/min under normal physiological conditions. The CentriMag may also be used to provide temporary right ventricular (RV) support after left VAD (LVAD) insertion and has FDA approval for use for up to 30 days for this indication. In a multicenter study, 38 patients with cardiogenic shock were supported

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with CentriMag, and overall 30-day survival was 47%.[26] Several studies have reported support with the CentriMag system for >100 days without any instances of pump failure or thromboembolic events.[27] Some centers are using the CentriMag device for ECMO support, allowing rapid initiation of biventricular support.

Percutaneous MCS

The TandemHeart (CardiacAssist, Inc, Pittsburgh, PA) is a nondurable, percutaneous, continuous-flow centrifugal pump with an external controller. It can be placed in the cardiac catheterization laboratory and generates up to 5 L/min of flow. This device uses transseptal left atrial inflow via a percutaneous femoral venous cannula and outflow via a contralateral femoral arterial cannula.[28,29] Removal of the device is done at the bedside or at the time of durable MCS surgery or transplantation. The device was designed to temporarily support patients during high-risk percutaneous interventions in the cardiac catheterization laboratory and has been used successfully for postcardiotomy HF and cardiogenic shock. This device is appealing as an alternative in patients with refractory cardiogenic shock because it has the potential to avoid the morbidity and mortality associated with surgical device placement. Complications of this device include bleeding, thrombosis, leg ischemia, and dislocation of transseptal or atrial cannulas. Support with the TandemHeart is reported to improve cardiac indexes, blood pressure, and mixed venous oxygen saturation[30] and to reverse the terminal hemodynamic compromise seen in patients with cardiogenic shock refractory to IABP and vasopressor support.[31]

The Impella 2.5 (ABIOMED, Inc) is a nondurable, percutaneous, continuous-flow, axial pump with an external controller. The simple design is a significant advantage for this device, allowing straightforward percutaneous insertion and rapid initiation of circulatory support in the catheterization laboratory. This device rests across the aortic valve and pumps up to 2.5 L/min of blood from the left ventricle to the ascending aorta. The Impella 2.5 may be used to support high-risk coronary angioplasty and for patients with myocardial infarction complicated by cardiogenic shock.[32] Compared with treatment with IABP, the Impella 2.5 device provided superior hemodynamic support and was both feasible and safe; however, there was no difference in 30-day mortality between the 2 groups. With a maximum flow of 2.5 L/min, the use of the Impella 2.5 may be limited in patients with a large body mass index (BMI) or in those who are in cardiogenic shock and require more flow. The Impella 5.0 is of the same design, is slightly larger, and is capable of delivering 5-L/min flow. The Impella 5.0 was approved by the FDA (April 2009) for providing temporary circulatory support; however, it requires a surgical cut-down on a peripheral artery for insertion. Complications of the Impella device include bleeding, thrombosis, and limb ischemia.[33,34]

Withdrawal of Nondurable MCS

Patients who receive nondurable MCS (either percutaneous or surgically placed) should always be evaluated for possible ventricular recovery, particularly in the setting of postcardiotomy shock, myocardial infarction, or myocarditis. Weaning can be performed by assessing clinical parameters (hemodynamics and echocardiographic left ventricular function) while MCS is temporarily reduced. Although uniform guidelines for weaning MCS do not exist, it is common practice to reduce flows by 0.5 L/min while simultaneously assessing the clinical status and hemodynamics. Ventricular recovery can be detected first by the presence of native ventricular ejection on the arterial or pulmonary artery wave forms. Subsequent confirmation of recovery of ventricular function is best performed by either transthoracic or transesophageal echocardiography. It is important to confirm the presence of adequate anticoagulation and to optimize hemodynamics with invasive monitoring before weaning MCS and explantation. Percutaneous MCS can be removed at the bedside unless a femoral cut-down is performed for placement. Surgically placed MCS devices are preferably removed in the operating room, although a variety of minimally invasive techniques are being developed to facilitate easier removal.

Clinical Perspective: Bridge to Recovery

To achieve the best short-term and long-term survival, MCS must be initiated in an appropriate and timely fashion.[35] Often, the patient with cardiogenic shock may also have multisystem organ failure and demonstrate an uncertain neurological status at the time of evaluation for MCS. In this situation, implantation of durable MCS is associated with poor outcomes and is not cost-effective. Implantation of nondurable MCS as a bridge to decision allows support until the clinical situation justifies the implantation of a more permanent device.[36]

An increasing number of centers are using nondurable MCS as a means to achieve clinical stability before transfer to a specialized advanced HF center for more definitive therapy. Quick and appropriate intervention with MCS can allow stabilization and facilitate safe patient transfer, ultimately improving patient survival in the setting of cardiogenic shock. A multidisciplinary approach and excellent communication between local hospitals and specialized MCS centers can make this an effective strategy.[37] It is particularly important that the advanced HF center is involved in planning for definitive therapy as early as possible, particularly before the performance of high-risk invasive procedures involving coronary angioplasty, cardiac surgery, or ventricular tachycardia ablation.

Two important questions must be considered in patients with acute cardiogenic shock who are potential candidates for permanent support: (1) Which patients will benefit from temporary MCS? (2) What modality of nondurable MCS should be used? Considering the ongoing rapid evolution of these devices with concomitant improvements in efficacy and safety, the recommendation is to use the device that is familiar to the team and can best serve the needs of the patient.

Bridge to Transplantation

The development of durable, implantable MCS devices was initially conceived as permanent support of the heart as an alternative to heart transplantation. However, FDA concerns about the long-term performance and safety largely restricted the initial use of implantable MCS devices to patients eligible

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Table 3. Devices Approved by the FDA for Long-Term MCS

Device	Manufacturer	Mechanism	Position	Indications	Portable
Thoratec pVAD	Thoratec	Pulsatile	R, L, or bilateral	BTT, BTR	Yes
Novacor	World Heart	Pulsatile	L	BTT, DT	Yes
Heartmate XVE	Thoratec	Pulsatile	L	BTT, DT	Yes
Heartmate II	Thoratec	Axial flow	L	BTT, DT	Yes
Abiomed TAH	ABIOMED	Pulsatile	Bilateral	BTT	Yes/No
CardioWest TAH	Syncardia	Pulsatile	Bilateral	BTT	No
Berlin EXOR Pediatric	Berlin	Pulsatile/pneumatic	R, L, or bilateral	BTT	No
DeBakey Child	MicroMed	Continuous	L	BTT, BTR	No

FDA indicates Food and Drug Administration; MCS, mechanical circulatory support; pVAD, percutaneous ventricular assist device, R, right; L, left; BTT, bridge to transplantation; BTR, bridge to recovery; DT, destination therapy; and TAH, total artificial heart.

for heart transplantation, not for patients as DT. This bias by clinicians and the FDA to limit MCS to transplant-eligible patients set the early stage for what has become the BTT indication. It also led to the regulatory pathway by which most long-term, implantable MCS devices are evaluated today. Devices with FDA approval for BTT are listed in Table 3 and described below.

Extracorporeal MCS

The Thoratec Paracorporeal Ventricular Assist Device II received FDA approval for BTT in 1995. With its smaller portable external driver, patients may be discharged from the hospital to await heart transplantation.[38] In a review of 84 patients in a single center, survival was reported to be 56%, with 79% of patients alive 1 year after heart transplantation.[39]

A single option for BTT in the pediatric population is the Berlin EXCOR VAD (Berlin Heart, GmbH, The Woodlands, TX), which was recently approved by the FDA. This device is an extracorporeal, pulsatile, pneumatic pump for left or biventricular support. In a report on its use in 73 children,[40] overall mortality was 23%, with younger age and need for biventricular support predicting mortality by multivariable analysis.

Implantable MCS

The Thoratec HeartMate vented electric XVE (Thoratec Corp) and the Novacor LVAD system (Novacor LVAS, Baxter, Oakland, CA)[41] were early implantable, pulsatile, pneumatic devices with small external controllers. These devices are largely historical and are not used today. Broad implementation of the pulsatile devices for BTT was limited by the large size of the implantable pumps and the risk of device failure (reported to be 35% at 24 months).[42]

The next generation of implantable MCS technology brought smaller and more durable devices. The current era includes continuous-, axial-, and centrifugal-flow devices.[43] The HeartMate II (Thoratec Corp) is an implantable, continuous, axial-flow device with a small external controller. This device has a single moving part and a much smaller profile than earlier HeartMate devices. The HeartMate II was approved by the FDA for BTT in April 2008. In a prospective, noncontrolled, multicenter trial including 281 patients, survival was 82% at 6 months and 73% at 12 months.[44] At 6 months, there was significant improvement in the 6-minute walk test, with the majority (83%) of patients in New York Heart Association (NYHA) functional class I or II. Improvement in quality of life was also recorded in patients treated as BTT. This device showed improved durability, with pump replacement required in only 4% of patients.[45]

The MicroMed DeBakey, a continuous, axial-flow pump, is not approved by the FDA for use in adults but is available for use in children 5 to 16 years of age. Because of its small size, the MicroMed DeBakey provides an important option for children for whom there are few alternatives for MCS.[46]

Total Artificial Heart

The earliest successes in MCS technology occurred with the total artificial heart. The original Jarvik 7–100 was used to support patients with severe HF, but its clinical application was limited by large device size and a high rate of stroke and infection. The CardioWest total artificial heart (Syncardia Systems Inc, Tucson, AZ) is an implantable, pulsatile, pneumatic pump with an external controller. It received FDA approval as a BTT in 2004[47] and is a modern version of the original Jarvik 7. In a multicenter trial, survival to transplantation was 79% among 81 patients supported with this device compared with 46% in the 35-patient historical medical therapy alone control group. Posttransplantation survival was superior for patients supported with the CardioWest total artificial heart (86% at 1 year, 64% at 5 years) compared with control subjects (69% at 1 year, 34% at 5 years). A portable driver for this device that would allow discharge from the hospital on support is under investigation. Development of the total artificial heart was eclipsed by the rapid growth of VAD technology; currently, the total artificial heart is reserved for patients who have severe biventricular failure and require MCS.

Clinical Perspective: BTT

The number of heart transplantations performed annually (2200 per year)[48] is much less than the number of patients with advanced HF. The emergence of MCS as BTT has clearly affected patient care, with 43% of all listed heart transplant recipients receiving MCS while awaiting a donor organ (http://www.srtr.org).[48]

Mortality among patients listed for heart transplantation is considerable, especially among the inotrope-dependent population, in whom 1-year survival is reported to be only 23%.[42] In these patients, the major advantages of MCS for BTT are

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improved survival, functionality, and quality of life. This may be particularly true for those predicted to have a long wait for an appropriate donor because of large body size, ABO blood type, or the presence of anti-HLA antibodies. Another benefit of MCS is the reversal (or prevention) of end-organ dysfunction from improved hemodynamics, including improvement in pulmonary hypertension.

A potential disadvantage of MCS for BTT is the need for additional surgery, an additional sternotomy, and repeat cardiopulmonary bypass. This may be a concern for patients with a prior cardiac surgery (previous valvular, coronary artery bypass graft, or congenital repairs). This history must be considered when a BTT strategy is adopted. Another concern is increased sensitization to HLA antibodies from exposure to blood products at the time of MCS implantation. This can be of considerable risk for those patients with preexisting HLA antibodies and can create an obstacle for finding a suitable donor match.[49] Complications of MCS, including infection, stroke, device failure, and thrombosis, can also affect ultimate candidacy for transplantation. Although early controversy existed in the literature on post-transplantation outcomes for patients supported with MCS as BTT,[50] recent reports suggest similar survival.[51,52] Appropriate patient selection and timing of MCS implantation are key to maximizing the benefit and minimizing the risk of MCS for BTT.

Destination Therapy

After the success of BTT in ambulatory patients with remarkable improvement in functional status and quality of life,[53] the use of MCS for DT was investigated. Early DT used the HeartMate XVE and Novacor devices; however, the HeartMate II is currently used almost exclusively.

The landmark trial that established DT as an indication for MCS was the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure Trial (REMATCH), a randomized, controlled trial of 129 nontransplantation candidates treated with either optimal medical management or support with the HeartMate XVE.[42] One-year survival rates for patients receiving DT and those receiving only optimal medical management were 52% and 23%, respectively. The 48% risk reduction in mortality led to FDA approval of the HeartMate XVE for DT in 2002. The HeartMate II was subsequently approved by the FDA for DT in January 2010 on the basis of a multicenter, randomized study that compared the HeartMate II and HeartMate XVE. On the basis of 200 transplantation-ineligible patients with advanced HF, survival in the HeartMate II cohort was 68% (1 year) and 58% (2 years) compared with 52% (1 year) and 24% (2 years) in the HeartMate XVE cohort. Compared with the medical management arm of the REMATCH trial in which survival was 25% (1 year) and 8% (2 years), the survival benefit of DT is appreciated.[54]

Clinical Perspective: DT

There are limited options for patients with advanced HF who are ineligible for heart transplantation, and these individuals face poor prognosis and limited quality of life. Even for patients receiving a high level of care (those enrolled in clinical trials), expected 6-month mortality is reported to be between 20% and 33%. In REMATCH, the 6-month mortality among patients requiring continuous inotropes was 61%.[55] Common contraindications to heart transplantation are advanced age, morbid obesity, pulmonary arterial hypertension, peripheral vascular disease, and severe diabetes mellitus. When these factors present a barrier for heart transplantation, alternative surgical options should be considered, especially for the younger patient. As described above, improved overall survival reported in the REMATCH clinical trial[42] and the later HeartMate II DT clinical trial[54] supported the use of DT.

In addition to improved survival, the majority of patients experience significant improvement in both functional status (NYHA classification and 6-minute walk tests) and quality of life (Minnesota Living With Heart Failure questionnaire and Kansas City Cardiomyopathy questionnaire) after MCS. In the HeartMate II DT clinical trial, 80% of patients had NYHA class I or II symptoms at 24 months and a doubling of the mean distance on the 6-minute walk test.[42,54] Patients selected for DT may have significant improvement of heart transplantation contraindications and ultimately be selected for transplantation.[56]

Table 4. Devices Currently Under Investigation for Long-Term MCS

Device	Manufacturer	Mechanism	Position
Jarvik 2000	Jarvik Heart	Axial flow	L
HeartWare HVAD	HeartWare	Centrifugal	L
Levacor	World Heart	Centrifugal	L
DuraHeart	Terumo	Centrifugal	L
Evaheart	Sun Medical	Centrifugal	L
Synergy	CircuLite	Axial/centrifugal	Other

MCS indicates mechanical circulatory support; L, left.

Devices Under Investigation

Currently, several devices are under active investigation (Table 4). The Jarvik 2000 Flow Maker (Jarvik Heart Inc., New York, NY) is an implantable, continuous, axial-flow device. Although it is similar in design to the HeartMate II, fundamental differences include intraventricular device positioning and the design capability to orient the outflow to the descending thoracic aorta via a left thoracotomy as opposed to a median sternotomy.[57] Additional continuous-flow devices undergoing clinical investigation in the United States include the MicroMed DeBakey (axial design for adult patients) and devices with centrifugal design such as HeartWare HVAD, Terumo DuraHeart, and Evaheart Medical Evaheart.[43,58] These devices feature magnetically levitated rotors and are proposed to have superior durability as a result of minimal wear. The HeartWare HVAD was recently studied for BTT in a multicenter trial, ADVANCE (EvAluation of the HeartWare LVAD System for the Treatment of AdVANCed Heart FailurE). Recently, Aaronson[58a] reported comparable 180-day survival in BTT patients supported with HeartWare HVAD compared with a concomitantly enrolled population in the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS). The HVAD rests

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within the pericardium and does not require creation of a preperitoneal pocket, which may reduce the likelihood of device infection. Experience with HeartWare HVAD for BTT and DT in Europe and Japan has resulted in 1-year survival rates between 77% and 86%.

Another innovation is the novel concept of long-term partial support. The Synergy Pocket Micro-Pump (CircuLite, Inc, Saddle Brook, NJ) provides partial support (≈3 L/min) and is intended to be implanted before patients meet current standard MCS criteria. This device is implanted in a right subclavian pacemaker pocket with outflow to the right subclavian artery.[59]

Identifying the High-Risk HF Patient

The cornerstone of successful therapy with MCS is timely and appropriate patient selection. This requires patient evaluation based on severity of HF, operative risk, psychosocial stability, and ability to adhere to the post-MCS self-care regimen. Proper identification of advanced HF patients with the highest mortality risk and subsequent appropriate referral for MCS are critically important. Practitioners involved in the care of patients with advanced HF should be able to identify and communicate relevant comorbid conditions and to inform patients of alternative treatment options.

Mortality Risk in the Outpatient Setting

Two statistical models are available for individual patient risk quantification: the Heart Failure Survival Score[60] and the Seattle Heart Failure Model.[61] The Heart Failure Survival Score identifies ambulatory patients with severe HF who are potential candidates for transplantation or MCS. The prognostic value of the Heart Failure Survival Score may be limited because it was devised in an era that preceded the use of spironolactone, defibrillators, and biventricular pacemakers. The Seattle Heart Failure Model was developed and validated among ambulatory patients; it predicts mean 1-, 2-, and 3-year survival in patients moderate HF (http://depts.washington.edu/shfm/). The Seattle Heart Failure score indicates that NYHA functional class, ischemic origin, diuretic dose, left ventricular ejection fraction, systolic blood pressure, serum sodium, hemoglobin, percent lymphocytes, uric acid, and cholesterol have independent predictive power.[61–64] This model is predictive of mortality in HF and may be used to identify at-risk patients.[65] The Seattle Heart Failure Model may overestimate survival when used to stratify advanced HF patients. Validation studies using patients considered for heart transplantation or MCS found the model to be better at predicting the single end point of death alone and less robust when predicting combined death, LVAD, or emergency transplantation. The hope is that the use of the Seattle Heart Failure Model in future clinical trials, including trials investigating MCS, will provide further validation.[66,67]

Mortality Risk in the Inpatient Setting

Among patients who are hospitalized for decompensated HF, mortality risk is influenced by many factors, including advanced age, hypotension, renal insufficiency, and hyponatremia.[68–70] The overall average in-hospital mortality for HF patients is described as 4.2%; however, this may be a gross underestimation or overestimation of the true mortality risk for an individual patient. The Acute Decompensated Heart Failure National Registry (ADHERE)[69] provides a predictive model for hospitalized patients based on 3 readily available variables at HF admission: systolic blood pressure <115 mm Hg, blood urea nitrogen ≥43 mg/dL, and serum creatinine ≥2.75 mg/dL (Table 5). In this analysis, the in-hospital mortality varies from 2.1% for the low-risk group to 21.9%, a dramatic 10-fold increase in mortality, for the high-risk group. The highest inpatient mortality occurs among hospitalized patients with cardiogenic shock.[71] Simply defined as end-organ hypoperfusion secondary to low cardiac output, patients with hepatic or renal insufficiency resulting from poor perfusion should be recognized as high risk. Finally, HF mortality increases significantly after each HF hospital admission[72] and is directly related to the duration and frequency of HF admissions.[73]

Table 5. In-Hospital Mortality Based on the ADHERE CART Model

Risk Group	In-Hospital Mortality, %
High risk	21.9
BUN ≥43 mg/dL	
SBP <115 mm Hg	
Creatinine ≥2.75 mg/dL	
Intermediate risk 1	12.4
BUN ≥43 mg/dL	
SBP <115 mm Hg	
Creatinine <2.75 mg/dL	
Intermediate risk 2	6.4
BUN ≥43 mg/dL	
SBP ≥115 mm Hg	
Intermediate risk 3	12.4
BUN <43 mg/dL	
SBP <115 mm Hg	
Low risk	2.1
BUN <43 mg/dL	
SBP ≥115 mm Hg	

ADHERE indicates Acute Decompensated Heart Failure National Registry; CART, classification and regression tree; BUN; blood urea nitrogen; and SBP, systolic blood pressure.

Patients with progressive symptoms, who have multiple admissions for HF, who are failing or intolerant of conventional HF therapy (including medical therapy and cardiac resynchronization), or who show signs of poor perfusion are at high risk of dying and should be considered candidates for advanced HF therapy with MCS and/or transplantation evaluation[3] (Table 6).

Patient Selection for MCS

Clinicians caring for a large population of HF patients are responsible for determining which patients should be referred for MCS. Patients with high mortality risk should be considered for advanced HF therapy. Often, it is not until the chronic HF patient becomes unstable that the mortality risk is recognized. Cardiogenic shock patients may require rapid

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Table 6. Prognostic Determinants in Advanced HF

Demographic
Advanced age
Male sex
Clinical
Frequent hospitalizations (>1 in past 6 mo)
Advanced NYHA class (III or IV)
Intolerance to neurohormonal antagonists
Increased diuretic requirement
Hypotension
Failed CRT
Inotrope dependence
Comorbidities (eg, diabetes mellitus, anemia, COPD)
Laboratory
Hyponatremia
Renal insufficiency (BUN/serum creatinine)
Hepatic insufficiency
Elevated neurohormones, natriuretic peptides, troponins, CRP
Doppler echocardiography and right-heart catheterization
Low LVEF (<30%)
Mitral regurgitation/increased left atrial volume
Increased filling pressure (PCWP >16 mm Hg or RAP>12 mm Hg)
Low RVEF
Increased pulmonary vascular resistance
Functional capacity
Inability to perform an exercise test
Low peak $V\dot{o}_2$ (<12–14 mL · kg^{-1} · min^{-1})
Increased ventilatory response to exercise ($V\text{E}/V\dot{c}o_2$ slope)
Low 6-min walk test distance (<300 m)

HF indicates heart failure, NYHA, New York Heart Association; CRT, cardiac resynchronization therapy; COPD, chronic obstructive pulmonary disease; BUN, blood urea nitrogen; CRP, C-reactive peptide; LVEF, left ventricular ejection fraction; PCWP, pulmonary capillary wedge pressure; RAP, right atrial pressure; and RVEF, right ventricle ejection fraction.

Adapted from Metra et al.[3]

Table 7. Indications and Contraindications to Durable Mechanical Support

Indications
Frequent hospitalizations for HF
Intolerance to neurohormonal antagonists
NYHA IIIb–IV functional limitations despite OMT
End-organ dysfunction owing to low CO†
Increasing diuretic requirement
CRT nonresponder
Inotrope dependence
Low peak $V\dot{o}_2$ (<14 mL · kg^{-1} · min^{-1})
Contraindications
Absolute
Irreversible hepatic disease
Irreversible renal disease
Irreversible neurological disease
Medical nonadherence
Severe psychosocial limitations
*Relative**
Age >80 y for DT
Obesity or malnutrition
MS disease that impairs rehabilitation
Active systemic infection or prolonged intubation
Untreated malignancy
Severe PVD
Active substance abuse
Impaired cognitive function
Unmanaged psychiatric disorder
Lack of social support

HF indicates heart failure; DT, destination therapy; NYHA, New York Heart Association; OMT, optimal maximal therapy; MS, musculoskeletal; CO, cardiac output; CRT, cardiac resynchronization therapy; and PVD, peripheral vascular disease.

*Relative contraindications warrant evaluation by advanced HF team.

†Cardiorenal syndrome, hepatic insufficiency, and pulmonary venous hypertension.

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stabilization with short-term MCS and then evaluation for extended MCS as appropriate.

The selection criteria for MCS are not static, and frequent reassessment of candidacy is required after changes in the patient's condition[42,74] (Table 7). The weighing of risk versus benefit is an iterative process that is affected by even small changes in the patient's physical condition or psychosocial/behavioral situation. In general, the first step to patient selection is the assessment of disease severity, followed by an operative risk assessment. Ultimately, confirmation of adequate psychosocial support and capacity for self-care is also crucial; without this element, a successful surgery could be rendered futile in the long run.

Assessment of Disease Severity: Too Sick Versus Too Well

INTERMACS is a US registry acquiring data on patients supported with FDA-approved MCS devices. Within INTERMACS, patients are classified by their signs and symptoms into 7 clinical profiles (Table 8).[75] This classification differentiates patients with NYHA class III to IV symptoms and provides a more detailed description of disease severity. The prognostic implications of the INTERMACS profiles provide guidance for the optimal timing of implantation and the associated risk based on clinical presentation (Figure 3). INTERMACS patient profile 1 is defined as critical cardiogenic shock, or crash and burn. These patients have the highest disease severity and highest risk of postimplantation mortality compared with patients presenting with less severe HF (ie, INTERMACS patient profiles 2–7). Patients receiving a durable MCS at INTERMACS patient profile 1 or 2 have a postimplantation mortality that is 44% greater than that of those receiving a long-term MCS at INTERMACS patient profile 3 or 4.[76] Patients with characteristics consistent with INTERMACS patient profile 1 qualify for MCS therapy based on disease severity; however, the presence of end-organ damage, neurological status, and other contributing factors may limit feasibility. Most frequently, death occurs as

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Table 8. INTERMACS Clinical Profiles

Level	Description	Hemodynamic Status	Time Frame for Intervention
1	Critical cardiogenic shock, "crash and burn"	Persistent hypotension despite rapidly escalating inotropic support and eventually IABP, and critical organ hypoperfusion	Within hours
2	Progressive decline on inotropic support, "sliding on inotropes"	Intravenous inotropic support with acceptable values of blood pressure and continuing deterioration in nutrition, renal function, or fluid retention	Within days
3	Stable but inotrope dependent, "dependent stability"	Stability reached with mild to moderate doses of inotropes but demonstrating failure to wean from them because of hypotension, worsening symptoms, or progressive renal dysfunction	Elective over weeks to months
4	Resting symptoms, "frequent flyer"	Possible weaning of inotropes but experiencing recurrent relapses, usually fluid retention	Elective over weeks to months
5	Exertion intolerant, housebound	Severe limited tolerance for activity, comfortable at rest with some volume overload and often with some renal dysfunction	Variable urgency, dependent on nutrition and organ function
6	Exertion limited, "walking wounded"	Less severe limited tolerance for activity and lack of volume overload, fatigue easily	Variable urgency, dependent on nutrition and organ function
7	Advanced NYHA III "symptoms, placeholder"	Patient without current or recent unstable fluid balance, NYHA class II or III	Not currently indicated

INTERMACS indicates Interagency Registry for Mechanically Assisted Circulatory Support; IABP, intra-aortic balloon pump; and NYHA, New York Heart Association. Adapted from Alba et al.[76]

a result of multisystem organ failure. Placement of a long-term MCS device for DT is not recommended in patients with an uncertain neurological status, sepsis, major coagulopathy, prolonged respiratory failure, irreversible major end-organ failure, or right-side HF.[77] The second annual report from INTERMACS demonstrated that fewer emergency implantations are performed in hemodynamically unstable patients, suggesting an emerging recognition of the mortality risk in this group.[78] A single-center study demonstrated an almost 3-fold improvement in survival after durable MCS for profile 3 and 4 patients compared with profile 1 and 2 patients ($P<0.05$).[76] Profile 6 or 7 patients, who by definition have advanced NYHA class III symptoms, are, in general, considered too well for MCS on the basis of current data. However, a clinical trial is now underway to investigate MCS in this group.[79] The INTERMACS classification scheme includes modifiers for arrhythmia, frequent hospital admissions, and temporary circulatory support, allowing increased consideration for patients affected by those factors that accelerate the risk of death. The HeartMate II LVAD is approved by the FDA for NYHA class IIIb and IV symptoms (INTERMACS profiles 1–5).

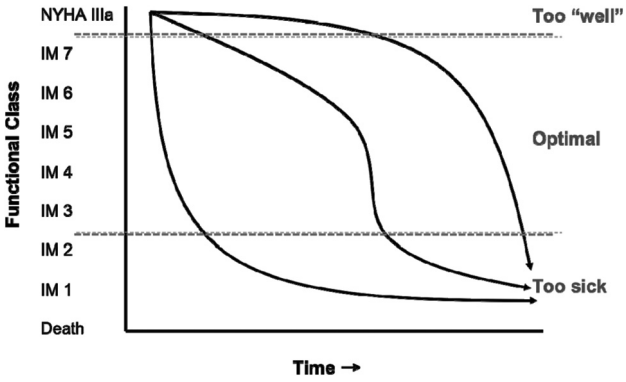

Figure 3. Optimal Timing for mechanical circulatory support. NYHA indicates New York Heart Association; IM, INTERMACS level.

Evaluating Operative Risk

A complete risk assessment for MCS begins with evaluation of HF acuity and severity, followed by assessment of comorbid conditions. Typically, the first step is determination of whether the patient is a candidate for heart transplantation. Discussion of heart transplantation candidacy is outside the scope of this statement but is detailed in the International Society for Heart and Lung Transplantation listing criteria.[60]

In general, selection criteria for patients being considered for MCS therapy as BTT follow the selection criteria for heart transplantation candidates. Selection criteria for MCS may be more liberal than those for heart transplantation, in some instances, in that one of the goals of MCS is stabilization or reversal of organ dysfunction or comorbidities to increase the likelihood of successful transplantation. Thus, reversible comorbidities that represent contraindications to heart transplantation may not be contraindications to MCS. Candidates for MCS may be subjected to less restrictive criteria in the hope that factors that represent contraindications to transplantation such as end-organ dysfunction, pulmonary hypertension, or nutritional deficiencies will reverse with MCS. Patients considered for DT, by definition, have contraindications for heart transplantation. However, 17% of DT recipients achieve improvement or resolution of contraindications to transplantation during MCS and ultimately receive a heart transplantation.[80]

Several single-institution and multi-institution databases provide descriptions of risk factors for mortality after MCS implantation. These include the Columbia University/Cleveland Clinic risk factor selection,[81] the revised screening scales,[74] the Muenster risk score, and INTERMACS.[82] The Lietz-Miller score (Table 9), a tool to assess longer-term mortality, was devised to estimate the survival after implantation of an LVAD for DT. Based on data from 280 patients who underwent implantation of the pulsatile HeartMate XVE LVAD from 2002 to 2005, multivariate analysis revealed 9 risk factors that predict mortality at 90 days.[80] A score >19 defines a patient for whom surgery may be futile. This risk

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Table 9. The Lietz-Miller Score for Preoperative Evaluation

	Weighted			Survival, %		
Patient Characteristic	Risk Score	Total Score	Risk Category	Discharge	90 d	1 y
Platelet count $<148\times10^3/\mu L$	7	0–8	Low	87.5	93.7	81.2
Serum albumin <3.3 g/dL	5	9–16	Medium	70.5	86.5	62.4
INR >1.1	4	17–19	High	26.0	38.9	27.8
Vasodilator therapy	4	>19	Very high	12.7	17.9	10.7
Mean PAP <25 mm Hg	3					
AST >45 U/mL	2					
HCT <34%	2					
BUN >51 mg/dL	2					
No intravenous inotropes	2					

INR indicates international normalized ratio; PAP, pulmonary artery pressure; AST, aspartate aminotransferase; HCT, hematocrit; and BUN, blood urea nitrogen.

Adapted from Leitz et al.[80]

model has not yet been validated with continuous-flow devices implanted for DT; however, many centers use the Lietz-Miller score for preoperative risk assessment for these patients. Other risk factors for poor outcome after LVAD implantation include severe chronic malnutrition, cardiac cachexia, extreme obesity, and history of noncompliance with the medical regimen.[41,53,77,83–89] Information on contraindications to MCS from these studies is limited by their size and lack of prospective validation of findings. Nonetheless, these studies provide insight into the issues to be considered in the assessment of a patient's suitability for MCS. There is a clear and immediate need for more prospective models to the guide the timing of and risk associated with implantation.

Major comorbid illness that is anticipated to limit a patient's survival to <2 years such as an advanced malignancy, severe liver disease (particularly if cirrhotic), severe lung disease (including pulmonary arterial hypertension that is not related to chronic HF, not World Health Organization group II), or a severe neurological or neuromuscular disorder should be viewed as a major contraindication to MCS.

Patient suitability for either heart transplantation or MCS (as BTT, bridge to decision, or DT) is ultimately determined by the implanting/transplanting center. Gaining understanding of this process and the most frequent contraindications for MCS is important for referring physicians. Increased awareness will ensure optimal timing for MCS evaluation (before it is too late) and allow collaboration in the early stages of patient selection for long-term MCS.

Complicating Conditions for MCS

RV Failure

RV failure after LVAD implantation is a serious complication, leading to an estimated 19% to 43% increase in perioperative mortality and decreased survival to transplantation.[86,90–92] Severe RV failure increases the cost of hospitalization, length of stay, morbidity, and mortality associated with surgery. Although biventricular support is available and feasible in some candidates, it is not practical in DT patients and complicates the long-term management of BTT patients. It follows that MCS may be contraindicated in a patient at high risk of irreversible RV failure who is not a candidate for biventricular support.

Pulmonary arterial hypertension with an elevated pulmonary vascular resistance (>5 Wood units) was once thought to predict RV failure after LVAD[93] because these factors are associated with poor outcome after heart transplantation. More recent studies suggest that depressed RV myocardial function is more accurately characterized by a low RV stroke work index, low pulmonary arterial pressure, and elevated right atrial pressure.[90,92,94,95] Patients with pulmonary hypertension who undergo MCS usually have improved pulmonary vascular resistance,[96,97] reduced pulmonary arterial hypertension, and similar posttransplantation survival compared with patients without preexisting pulmonary arterial hypertension.[98–101] Thus, pulmonary hypertension should not be considered an absolute contraindication to MCS.

Preoperative echocardiographic assessment of RV function is important, and the appearance of RV enlargement and hypokinesis typically raises concern. To quantify RV contractility, the RV stroke work index can be calculated by the following formula: (mean pulmonary artery pressure−mean right atrial pressure)×stroke volume/body surface area. An RV stroke work index <300 mm Hg · mL · m^{-2}, white blood cell count $>10.4\times10^3$/mL, central venous pressure >15 mm Hg, and hematocrit <31% were found to be associated with RV failure after LVAD implantation.[102] Fitzpatrick et al[103] demonstrated that risk scoring with points assigned for decreased RV stroke work index, low cardiac index, severe RV dysfunction (by echocardiography), elevated creatinine, previous cardiac surgery, and systolic blood pressure ≤96 mm Hg predicts the need for RV support. Another risk score[104] found vasopressor requirement and elevated aspartate aminotransferase, bilirubin, or creatinine to predict RV failure and mortality. These models suggest that patients with a greater degree of both end-organ and RV dysfunction are more likely to need biventricular support. Factors that predispose to high blood transfusion requirement such as reoperation, hepatic dysfunction, and coagulopathy increase the likelihood of RV distention and failure. Perioperative management that includes possible tricuspid annuloplasty for moderate to severe tricuspid regurgitation and the use of selective pulmonary vasodi-

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lators (nitric oxide, prostanoids, or type 5 phosphodiesterase inhibitors) may attenuate the development of early RV failure.[105] The early use of biventricular support in the patient at high risk of RV failure should be considered because survival is better with planned RV support as opposed to salvage RV assist device implantation.[103] Patients with RV failure are at risk for a more complicated perioperative and postoperative course and overall higher mortality as they await transplantation.[82,106,107]

Structural Heart Disease

Structural heart disease that prohibits a successful implantation may also be a contraindication to MCS.[108] Hypertrophic, infiltrative, or restrictive cardiomyopathy may represent a relative contraindication, although select patients may benefit from MCS. A recent small study from the Mayo Clinic showed comparable 1-year survival among 8 patients with restrictive or hypertrophic cardiomyopathy compared with 75 patients with dilated and ischemic cardiomyopathy.[109] Most patients with complex congenital heart disease are not candidates for MCS, although a careful preoperative consideration of an individual patient's anatomy may permit successful implantation in highly selected cases.[110]

Aortic Valve Disorders

Because of the possible development of a closed loop of LVAD flow, patients with uncorrectable moderate or greater aortic insufficiency should not undergo durable MCS unless the insufficiency is corrected by aortic valve repair or replacement with a bioprosthetic valve or the aortic valve is sewn shut. It should be noted that patients who have their aortic valves oversewn or who have subsequent fusion of prosthetic valve leaflets or native leaflets are completely dependent on the LVAD support; disruption of device function could be fatal.[111,112] Bioprosthetic valves are preferred in patients who require aortic valve replacement in this setting because there is increased risk of thrombosis with mechanical aortic valves. In patients with a preexisting mechanical aortic prosthesis, subvalvular stasis can lead to thrombosis in the case when the ventricle is not ejecting.[113,114] Although successful durable MCS for several months in patients with mechanical aortic prostheses has been reported,[115] in general, these prostheses are replaced with a bioprosthetic valve or prosthetic patch placed above the mechanical valve.[113] Aortic stenosis is not detrimental during device support because systemic flow occurs through the device rather than across the aortic valve. Therefore, it is not essential that aortic stenosis be corrected.

Mitral Valve Disorders

Mitral insufficiency does not need to be repaired in most cases.[77] In general, unloading of the ventricle may improve mitral regurgitation that is secondary to annular dilatation from left ventricular enlargement. Mitral stenosis may compromise filling of the LVAD. Therefore, when significant, mitral stenosis is typically corrected before LVAD implantation. Patients with prosthetic mitral valves before the VAD surgery may require a higher level of anticoagulation but do not need additional mitral surgery.

Tricuspid Valve Disorders

Tricuspid regurgitation may cause or exacerbate RV failure. The general consensus is that severe tricuspid insufficiency should be repaired at the time of LVAD implantation.[77]

Shunts

Unrecognized patent foramen ovales or atrial septal defects can contribute to hypoxemia from right-to-left shunting after VAD implantation and paradoxical emboli. Investigation for a shunt should be performed before surgery or intraoperatively, and repair should be performed during LVAD implantation.

Hepatic Dysfunction

HF can cause hepatic dysfunction via decreased hepatic blood flow, increased hepatic venous pressures, and decreased arterial oxygen saturation.[116] The associated coagulopathy of liver disease and hepatic congestion may increase the need for blood transfusions during the intraoperative and perioperative periods. Optimization of hemodynamics with reduction of pulmonary vascular resistance, reduction of right atrial pressures, improvement of cardiac output, and correction of coagulopathies should be pursued before MCS.

Vasodilators may be used to improve preload, afterload, and pulmonary vascular resistance, which may alleviate hepatic congestion. Ultrafiltration can also provide relief of congestion. IABP or even a temporary assist device may be required to improve forward flow, thereby alleviating congestion. Hepatology consultation and measurement of hepatic venous pressure and liver biopsy should be considered to evaluate the degree of hepatic fibrosis.[117]

Vitamin K deficiencies should be evaluated and corrected with the use of supplemental vitamin K if needed.[118] Hypoproteinemia may exist and impede wound healing. Aggressive management with dietary consultation and nutritional supplementation should be pursued. Exclusion of noncardiac causes of hepatic dysfunction is also imperative and may require liver biopsy. Liver dysfunction resulting from HF may improve with MCS, and improvement of liver function has been demonstrated with both pulsatile- and continuous-flow devices.[119–122]

Kidney Dysfunction

Currently, there is no agreed-on glomerular filtration rate below which durable MCS should not be considered. Postoperative kidney failure after durable or nondurable MCS surgery is associated consistently with worse outcomes, including increased mortality and decreased rates of successful BTT.[74,123,124] Postoperative kidney failure is also associated with higher rates of other complications, including sepsis and longer lengths of intensive care unit and hospital stays.[124] Older age is the only known risk factor for postoperative kidney failure.[123,124]

Kidney dysfunction generally improves after durable MCS if the baseline impairment is secondary to low cardiac output or renal venous congestion.[122,125] Even the requirement of renal replacement therapy immediately postoperatively may be transient.[126] Many patients requiring postoperative continuous veno-venous hemofiltration or dialysis will have improvement in kidney function in the first few months after

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implantation and can be weaned from renal replacement therapy. Patients with chronic kidney dysfunction secondary to chronic poor perfusion, hypertension, or diabetes mellitus may not have improvement in function after durable MCS.

Although kidney dysfunction is not an absolute contraindication for MCS, caution should be exercised when durable MCS is considered in a patient with severe intrinsic renal disease. There are a number of limitations to providing long-term renal replacement therapy to patients requiring MCS. Infection is a major cause of morbidity in patients with end-stage renal disease requiring dialysis.[127] Given that device-related infections remain a significant cause of morbidity in patients supported with MCS,[128] patients requiring long-term dialysis should not be considered for durable MCS therapy. Additionally, few outpatient dialysis centers want to accommodate patients supported by durable MCS, particularly given the challenges of blood pressure monitoring in patients with continuous-flow devices. In some patients, home hemodialysis may be an option. However, by and large, the lack of outpatient dialysis resources may preclude centers from discharging a durable MCS patient requiring long-term renal replacement therapy to home. This issue needs additional experience and study.

Coagulopathy

Bleeding complications were common with the use of first-generation MCS. The REMATCH trial used a pulsatile-flow device (HeartMate XVE) that permitted lower-intensity anticoagulation, with the majority of patients taking antiplatelet agents alone[129]; only 38% of patients received systemic anticoagulation. Nonetheless, bleeding complications occurred frequently (0.56 events per patient-year).[42] The current generation of continuous-flow VADs may require both systemic anticoagulation and antiplatelet therapy. Bleeding problems have become more prominent than strokes with these newer continuous-flow devices. Such therapy resulted in a 3% mortality rate from bleeding in a long-term study of the HeartMate II VAD[77] despite an effort to exclude patients anticipated to be intolerant of anticoagulation. The propensity for bleeding in patients supported by continuous-flow devices may be driven by acquisition of a von Willebrand syndrome because of the effect of shear forces on the von Willebrand multimer.[130] This bleeding is typically manifest as mucosal bleeding observed primarily from arteriovenous malformations in the gastrointestinal tract. In 1 study, durable MCS support with a continuous-flow device was associated with 63 transfusion-requiring events per 100 patient-years.[131]

Thus, careful consideration of bleeding risk is essential. Patients with significant underlying coagulopathy, either an international normalized ratio $\geq$2.5 or a platelet count $<$50 000, should be excluded from durable MCS. A history of bleeding diathesis, even if manifest only during anticoagulation, should be considered a significant contraindication to MCS. A contraindication to anticoagulation is a contraindication to MCS in most situations. A thorough exploration of the gastrointestinal system, often including upper and lower endoscopy, should be considered for durable MCS candidates.

Malnutrition and Debilitation

The nutritional status of a MCS candidate is important because anorexia and cachexia often complicate advanced HF. Patients with malnutrition are predisposed to impaired healing, immune system dysfunction, infection, and higher mortality.[80,132] Patients with a preoperative serum albumin level $<$3.5 g/dL, a total protein level $<$6.0 g/dL, or an absolute lymphocyte count $<0.85\times10^3$/mL^3 are observed to have poor clinical outcomes, including a higher rate of sepsis, lower BTT rate, and longer intensive care unit length of stay.[90,124] Prealbumin, transferring, and low cholesterol can also be helpful markers of nutritional status. Patients demonstrating poor nutritional status should optimally undergo a period of nutritional supplementation based on their individual caloric and substrate needs before implantation.[77,133]

Obesity

Obesity is associated with a poor outcome after heart transplantation, and morbid obesity is frequently a contraindication to heart transplantation.[134] Because the incidence of HF is high among obese individuals, a large number of obese patients who are ineligible for heart transplantation are considered for DT.

Despite early concern for negative outcomes as a consequence of obesity, these fears were not borne out in experience. Butler et al[135] found no adverse impact on survival from increased BMI in an analysis of 22 patients. Coyle and colleagues[136] demonstrated that survival, NYHA classification, and renal function of obese patients (BMI $>$30 kg/m^2) were comparable to those in a similar group of nonobese patients (BMI $<$30 kg/m^2). This was also consistent with the findings of Musci and colleagues[132] that there was no significant difference in rate or cause of death among 5 BMI groups ($<$20, 20–24, 25–29, 30–34, and $>$35 kg/m^2) comprising 590 patients.

Infection risk among obese patients has received considerable attention because driveline exit site integrity can be challenging for the obese patient. The literature is equivocal on this issue; 1 report suggests no difference in driveline exit site infections,[137] and another suggests an increased risk among obese patients and those who gain weight after implantation.[138] Caution should be exercised in considering patients with extreme obesity (BMI $>$35 kg/m^2) for MCS because a greater 30-day mortality associated with multisystem organ failure has been observed.[132] As in all patients with a cardiac history, a low-fat, low-cholesterol, low-sodium diet remains the standard recommendation. Aggressive efforts combining nutritional and behavioral counseling with a regular, monitored exercise program (eg, phase III cardiac rehabilitation) should be undertaken to achieve weight loss in obese patients. Although MCS is considered in patients with a BMI too high for transplantation eligibility, many with continuous-flow LVAD do not lose weight after implantation.[139]

Psychosocial and Behavioral Issues

Self-care after durable MCS implantation requires considerable sophistication with requisite attention to sterile driveline exit site care, coordination with maintaining/alternating

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power source, and knowledge of emergency procedures in case of device alarms. Adherence to a complicated HF medical regimen may predict success; however, because of the technical complexity of durable MCS, additional considerations are required in the assessment of psychosocial and behavioral readiness for MCS.[140,141] The specific components of the psychosocial evaluation have received relatively little attention in the MCS literature. In general, it has been proposed that the factors typically evaluated in potential transplantation candidates also be included in the evaluation of candidates for MCS through the use of a multidisciplinary approach.[140,141] Assessment of psychiatric disorders, substance abuse, cognitive function, and ability to understand MCS care requirements; past and current levels of adherence to medical regimens; social history; visual or hearing impairment; musculoskeletal discoordination; and personal expectations and preferences are critical components of MCS evaluation because they may adversely affect posttransplantation outcomes. Financial resources for out-of-pocket expenses such as travel, dressing supplies, and temporary housing must also be assessed before implantation. After surgery, patients require caregiver support for MCS management, so a careful assessment of the availability of caregivers is essential for a safe discharge to home. In addition, patients need to be discharged to a safe, clean environment, so the assessment of housing with dependable electricity is also crucial.

Regulatory Issues: Modern Application of MCS

MCS remains a new and rapidly evolving field, applying an expensive technology to a critically ill patient population. In its current state of evolution, important benefits of MCS technology are to prolong and improve the quality of life. Regulatory mechanisms are positioned to ensure safe and appropriate application of MCS, specifically regarding DT. Mentioned previously, INTERMACS is a collaborative effort among the National Heart, Lung, and Blood Institute, the FDA, the Centers for Medicaid and Medicare Services, and the MCS professional community.[142] All implanting centers that are approved by the Centers for Medicare and Medicaid for DT are mandated to participate in this registry and to pay a fee to do so. Currently, >120 programs contribute MCS data to INTERMACS. Review of INTERMACS data provides the opportunity to monitor the growth of MCS as this technology evolves from specialized clinical trial centers to a wide variety of centers across the nation.

In March 2007, the Centers for Medicare and Medicaid mandated a disease-specific certification program for VADs. All implanting centers must receive certification from The Joint Commission. This is a national coverage determination meaning that centers cannot receive reimbursement from the Centers for Medicare and Medicaid for DT unless certified by The Joint Commission. This regulation provides an additional level of oversight. Mandatory participation in INTERMACS and the requirement for accreditation require significant administrative infrastructure and are a potential hurdle for new programs wishing to provide MCS therapy.

Conclusions

From the early days of mechanical support for cardiopulmonary bypass to modern-day MCS with percutaneous and fully implantable devices, advancement in this field has been remarkable. Significant challenges along the way fueled technological innovation, bringing more versatile and durable options for support. The REMATCH trial established durable MCS as an alternative to medical management for advanced HF[42,53]; however, the technology was not broadly implemented because of complications, including device failure. With the emergence of the next generation of durable fully implantable devices,[54] fewer adverse events and improved clinical outcomes stimulated rapid growth in the field. Looking forward, appropriate patient selection with a focus on earlier referral and optimization of comorbid conditions is anticipated to improve patient outcomes.

Recommendations for MCS

1. **MCS for BTT indication should be considered for transplant-eligible patients with end-stage HF who are failing optimal medical, surgical, and/or device therapies and at high risk of dying before receiving a heart transplantation (*Class I; Level of Evidence B*).**
2. **Implantation of MCS in patients before the development of advanced HF (ie, hyponatremia, hypotension, renal dysfunction, and recurrent hospitalizations) is associated with better outcomes. Therefore, early referral of advanced HF patients is reasonable (*Class IIa; Level of Evidence B*).**
3. **MCS with a durable, implantable device for permanent therapy or DT is beneficial for patients with advanced HF, high 1-year mortality resulting from HF, and the absence of other life-limiting organ dysfunction; who are failing medical, surgical, and/or device therapies; and who are ineligible for heart transplantation (*Class I; Level of Evidence B*).**
4. **Elective rather than urgent implantation of DT can be beneficial when performed after optimization of medical therapy in advanced HF patients who are failing medical, surgical, and/or device therapies (*Class IIa; Level of Evidence C*).**
5. **A. Urgent nondurable MCS is reasonable in hemodynamically compromised HF patients with end-organ dysfunction and/or relative contraindications to heart transplantation/durable MCS that are expected to improve with time and restoration of an improved hemodynamic profile (*Class IIa; Level of Evidence C*).**
   B. These patients should be referred to a center with expertise in the management of durable MCS and patients with advanced HF (*Class I; Level of Evidence C*).
6. **Patients who are ineligible for heart transplantation because of pulmonary hypertension related to HF alone should be considered for bridge to potential transplant eligibility with durable, long-term MCS (*Class IIa; Level of Evidence B*).**

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7. **Careful assessment of RV function is recommended as part of the evaluation for patient selection for durable, long-term MCS (*Class I; Level of Evidence C*).**
8. **A. Long-term MCS is not recommended in patients with advanced kidney disease in whom renal function is unlikely to recover despite improved hemodynamics and who are therefore at high risk for progression to renal replacement therapy (*Class III; Level of Evidence C*).**
   B. Long-term MCS as a bridge to heart–kidney transplantation might be considered on the basis of availability of outpatient hemodialysis (*Class IIb; Level of Evidence C*).
9. **Assessment of nutritional status is recommended as part of the evaluation for patient selection for durable, long-term MCS (*Class I; Level of Evidence B*).**
10. **Patients with obesity (BMI ≥30 to ≤40 kg/ m^2) derive benefit from MCS and may be considered for long-term MCS (*Class IIb; Level of Evidence B*).**
11. **Assessment of psychosocial, behavioral, and environmental factors is beneficial as part of the evaluation for patient selection for durable, long-term MCS (*Class I; Level of Evidence C*).**
12. **Evaluation of potential candidates by a multidisciplinary team is recommended for the selection of patients for MCS (*Class I; Level of Evidence C*).**

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Writing Group Disclosures

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
Jennifer L. Peura	Medical University of South Carolina	None	None	None	None	None	None	None
Monica Colvin-Adams	University of Minnesota	HeartWare*; Thoratec*	None	None	None	None	None	None
Gary S. Francis	University of Minnesota	None	None	None	None	None	None	None
Kathleen L. Grady	Northwestern University	None	None	None	None	None	None	None
Timothy M. Hoffman	Nationwide Children's Hospital	None	None	None	None	None	None	None
Mariell Jessup	University of Pennsylvania	HeartWare†; Thoratec†	None	None	None	None	None	None
Ranjit John	University of Minnesota	HeartWare†; Levitronix†; Thoratec†	None	None	None	None	None	None
Michael S. Kiernan	Tufts Medical Center	None	None	None	None	None	None	None
Judith E. Mitchell	SUNY Downstate Medical Center	None	None	None	None	None	None	None
John B. O'Connell	Medical Center of Central Georgia in Macon	Thoratec†	None	Thoratec*	None	None	World Heart*	None
Francis D. Pagani	University of Michigan	HeartWare*; Terumo*; Thoratec*	None	None	None	None	None	None
Michael Petty	University of Minnesota Medical Center, Fairview	Thoratec*; Ventracor Ltd*	None	Thoratec*	None	None	None	None
Pasala Ravichandran	VA Medical Center	None	None	None	None	None	None	None
Joseph G. Rogers	Duke University	None	Thoratec*	None	None	None	Thoratec†	None
Marc J. Semigran	Massachusetts General Hospital/Harvard Medical School	None	None	None	None	None	None	None
J. Matthew Toole	Medical University of South Carolina	None	None	None	None	None	None	None

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*Modest.

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Reviewer Disclosures

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Bernice L. Coleman	Cedars Sinai Medical Center	None	None	None	None	None	None	None
Sudhir S. Kushwaha	Mayo Clinic	Thoratec†	None	None	None	None	None	None
Leslie W. Miller	University of South Florida	HeartWare DT trial*	None	None	None	None	None	None
Maria Mountis	Cleveland Clinic	None	None	None	None	None	Thoratec*	None
Randall Carson Starling	Cleveland Clinic	Novartis†; Biotronik†; NIH†	None	Medtronic*; Novella*; BioControl*	None	Cardiomems*	Thoratec member publications committee*	None
Connie White-Williams	University of Alabama Medical Center	None	None	None	None	None	None	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

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KEY WORDS: AHA Scientific Statements ■ cardiomyopathy ■ cardiovascular surgery ■ congestive (heart failure) ■ heart failure ■ mechanical circulatory support ■ pulmonary circulation and disease ■ transplantation ■ ventricular assistance

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