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Durable left ventricular assist device therapy in advanced heart failure: Patient selection and clinical outcomes

Sachin P. Shah [a,b,c,d], *Mandeep R. Mehra* [a,b,*]

[a] *Center for Advanced Heart Disease, Brigham and Women's Hospital Heart and Vascular Center, Boston, MA, United States*

[b] *Harvard Medical School, Boston, MA, United States*

[c] *Division of Cardiovascular Medicine, Lahey Hospital and Medical Center, Burlington, MA, United States*

[d] *Tufts University School of Medicine, Boston, MA, United States*

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ABSTRACT

The increasing adoption of left ventricular assist devices (LVADs) into clinical practice is related to a combination of engineering advances in pump technology and improvements in understanding the appropriate clinical use of these devices in the management of patients with advanced heart failure. This review intends to assist the clinician in identifying candidates for LVAD implantation, to examine long-term outcomes and provide an overview of the common complications related to use of these devices.

The increasing adoption of left ventricular assist devices (LVADs) into clinical practice is related to a combination of engineering advances in pump technology and improvements in understanding the appropriate clinical use of these devices in the management of patients with advanced heart failure. This review intends to assist the clinician in identifying candidates for LVAD implantation, to examine long-term outcomes and provide an overview of the common complications related to use of these devices. In the early 1990s, larger pulsatile LVADs (i.e. Novacor LVAD and Thoratec HeartMate XVE) were initially used for left ventricular support in patients awaiting cardiac transplantation. This strategy was not based on randomized data but was adopted out of necessity, given the long waiting times for cardiac transplantation.[1] As confidence grew, the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial was launched, which randomized 129 nontransplant candidates with end-stage heart failure to ongoing medical therapy (72% of patients supported with continuous intravenous inotropes) versus a pulsatile HeartMate XVE and demonstrated a dramatic survival advantage at one year (53% survival in the LVAD group and 25% survival in the medical therapy group).[2] This affirmed the proof of concept and viability of lifetime or destination therapy using mechanical circulatory support (MCS) systems. The initial adoption of pulsatile devices was low due to lesser device durability and frequent morbidity, but as LVAD technology advanced, the advent of smaller and more reliable continuous flow devices (HeartMate II LVAD and HeartWare HVAD) led to a dramatic rise in utilization of LVADs in the past decade. In 2013, the

* *Corresponding author.*
E-mail address: MMEHRA@BWH.HARVARD.EDU (M.R. Mehra).

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number of durable MCS devices in the United States ($n = 2642$, 97% continuous flow LVADs, 44% for destination therapy) exceeded the number of cardiac transplants performed.[3,4] For the past decade, the number of cardiac transplants per annum worldwide has remained stagnant at around 4000 related to the relatively fixed donor pool, with the vast majority of cardiac transplants being performed in the United States and Europe. Attempts at increasing the donor pool have been outpaced by the improving clinical outcomes experience with current generation LVADs contributing to a growing population of transplant ineligible patients supported with these devices as destination therapy. Balancing the risk–benefit ratio to match the device to the patient's condition will be paramount in prolonging and improving life while achieving cost-effectiveness.[5]

1. Patient selection

1.1. *Selecting patients with the appropriate severity of heart failure*

Determining a level of severity of illness in patients with advanced heart failure relies heavily on the degree of symptoms, refractoriness to traditional disease modifying therapy, and the worsening hemodynamic profile. As advanced-stage heart failure sets in, the traditional New York Heart Association classification system is no longer sufficient to characterize patients. Thus, the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profile system assigns a level (INTERMACS level 1 through 7) to patients based on the severity of illness (Table 1). Currently, the majority of patients undergoing LVAD implantation are either categorized as INTERMACS level 1 (critical cardiogenic shock), level 2 (progressive decline on inotropic therapy), or level 3 (stable but inotropic therapy dependent).[3] INTERMACS level 1 patients (those in critical cardiogenic shock) pose a challenge to LVAD implantation. Specifically, there is an increased risk of perioperative mortality (relative risk 1.55).[6] In response to the realization of the perioperative risk in patients with cardiogenic shock, the proportion of patients undergoing durable MCS implantation at INTERMACS level 1 has decreased over the past decade.[3,6,7] This increased risk is at least in part related to the end-organ dysfunction associated with cardiogenic shock and the inflammatory state of severe shock, leading to increased postimplant bleeding, infection, multisystem organ failure, and need for right heart support. Avoidance of support is not an adequate strategy and management algorithms in INTERMACS I patients have evolved to use temporary MCS devices, such as intra-aortic balloon counter-pulsation, percutaneous or surgical centrifugal devices (TandemHeart, Centrimag), percutaneous axial flow devices (Impella), or venoarterial extracorporeal membrane oxygenation (VA ECMO) in an effort to restore end-organ perfusion, stabilize the patient, and potentially reduce the risk of subsequent durable LVAD implantation.[8]

In general, patients with cardiogenic shock who can be stabilized with percutaneous support may be candidates for a durable LVAD, whereas patients who suffer from irreversible end-organ dysfunction (renal, hepatic, neurologic, etc.) or refractory shock despite temporary MCS are likely at higher risk and are suboptimal candidates for LVAD implantation.

Patients who are inotropic therapy dependent (INTERMACS levels 2 and 3) currently represent nearly two-thirds of all LVAD implantations and likely also represent the most appropriate use of the current technology. Patients treated with inotropic therapy due to refractory end-organ hypoperfusion or refractory symptoms related to advanced heart failure have an overall very poor prognosis with medical therapy alone. Of the 61 patients in the medical therapy arm of the REMATCH trial, 72% of patients were on continuous inotropic infusion, and by one year, only 25% of medically treated patients were alive, which decreased to 8% by two years.[2] The Investigation of Non-Transplant Eligible Patients who are Inotrope Dependent (INTrEPID) and Continuous Outpatient Support with Inotropes (COSI) trials are two other small prospective analyses, which demonstrated a 1-year survival of 11% and 6%, respectively in patients bound to continuous inotropic therapy support.[9,10] In contrast, the expected one-year survival of patients following implantation of a continuous flow LVAD now approaches 80% (Fig. 1).[6] Although the patient populations in these trials differ, these data infer a dramatic survival advantage for durable MCS in INTERMACS levels 2 and 3 patients with advanced heart failure.

Patients in INTERMACS levels 4 through 7 suffer from advanced heart failure but are not inotrope dependent. Not only are patients with this severity of illness more difficult to define, it is possible for an individual patient to transition between levels over time. Currently, only 18.5% of patients who undergo durable MCS are levels 4 through 7 (mostly INTERMACS level 4).[6] Of these patients, the INTERMACS 4 profile is increasingly gaining acceptance as an appropriate candidate group. Such patients exhibit symptoms of dyspnea and fatigue on minimal activity, are typically house bound due to the severity of symptoms, and suffer from a poor quality of life and excess 1-year mortality. The recently concluded ROADMAP trial provides insight into the selection of patients for LVAD therapy from this group of individuals.[11] Further estimation of prognosis in this ''less sick'' patient population is warranted with the use of other prognostic indicators in chronic heart failure, many of which are listed in Table 2.[12–19]

Table 1 – Current distribution of durable mechanical circulatory support devices across INTERMACS levels.

INTERMACS Level	Definition	% Of durable MCS
1	Critical cardiogenic shock	14.3%
2	Progressive decline	36.0%
3	Stable but inotrope dependent	29.6%
4	Resting symptoms	14.5%
5	Exertion-intolerant	3.0%
6	Exertion-limited	1.2%
7	Advanced NYHA Class 3	0.7%

INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; MCS, mechanical circulatory support; NYHA, New York Heart Association.