



# Are We Ready to Implant Left Ventricular Assist Devices In “Less Sick” Patients?

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Left ventricular assist devices improve survival for New York Heart Association class IV patients as both destination therapy and bridge-to-transplant therapy. This clinical benefit has been demonstrated in multiple clinical trials whose medical comparator arm consists of patients with very poor survival. This article discusses the potential use of left ventricular assist devices in a less sick group of patients with end-stage congestive heart failure.

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## ARE WE READY TO IMPLANT LEFT VENTRICULAR ASSIST DEVICES IN LESS SICK PATIENTS?

Despite innovative engineers and surgeons and courageous patients, the field of mechanical circulatory support has been slow to have a clinical impact on the ever-growing number of patients with end-stage congestive heart failure (esCHF). It is only during the last 2 years that the use of implantable left ventricular assist devices (LVADs) has shown significant growth. Currently, LVADs are primarily used in an easily identified group of patients, those who are deteriorating rapidly despite inotropes in or out of the intensive care unit. However, to meaningfully affect the epidemiology of esCHF, LVADs need to be used in a wider group of patients whose survival benefit might be smaller but whose primary benefit might be quality of life. There are no randomized trials comparing this group of medically treated less sick patients with LVAD implantation. However, there is already a subtle paradigm shift toward implanting the less sick patient. INTERMACS (IM) is a registry used to collect data on patients treated with Food and Drug Administration approved devices. During the last 5 years, it has demonstrated a de-

crease in the most severe profile (IM 1) and an increase in the less sick IM 4-7.<sup>1</sup>

Any discussion on LVADs for the less sick CHF patient must first address whether devices are ready for this population. The first generation of devices approved for destination therapy (DT) and bridge-to-transplant therapy (BTT) were pulsatile flow pumps. They provided excellent left ventricular decompression with pulsatility and minimal need for anticoagulation. However, they were large and had limited durability of about 14 months. This limited their adoption by both patients and physicians. The approval of continuous flow devices, specifically the Thoratec (Pleasanton, CA) HeartMate II, dramatically changed the risk profile with an improvement in durability and decrease in infection. It is not unusual to now see patients supported for more than 6 years from their initial pump implant date. Bearing wear is proving to be negligible in HeartMate II devices. Some devices in trials such as the Heartware (Framingham, MA) HVAD have no bearings and are “wearless.” Unless there is electrical failure, these devices could mechanically outlive patients. The small size of the devices and thinner, more flexible drivelines have decreased the overall device infection rate, which is the primary complication that limits the overall effectiveness of these devices. Once an infection occurs, a rescue transplant is the only cure. Device exchanges and driveline repositioning only suppress infection until resistant organisms lead to life-threatening sepsis. Infection rates have decreased dramatically from nearly 50% in the first year to as low as 5% in some centers. Smaller intrapericardial devices such as the HVAD have shown even lower infection rates. Furthermore, the battery

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life between recharges is now approaching 14 hours, which decreases the burden of accessories the patients need to carry with them. These improvements make the risks and maintenance associated with these devices more tolerable for the less sick patient.

#### WHAT IS THE DEFINITION OF THE LESS SICK PATIENT?

Most classifications such as the IM profile focus on the symptoms associated with cardiac dysfunction. However, significant comorbidities (such as renal, liver, nutritional, abnormalities) and technical issues (multiple sternotomies, valvular or coronary lesions) also should be considered when classifying patients. Although there are clinical trial data on a wide range of illness severity for LVAD implants, data on a comparable group of medically treated patients are lacking. Currently accepted indications for LVADs include New York Heart Association (NYHA) IV symptoms despite optimal medical management, left ventricular ejection fraction <25%, and peak oxygen consumption of <12 mL/kg/min or inotrope dependency.<sup>2</sup> This fits into IM 1-3. The ambulatory, non-inotrope-dependent, NYHA class IV patients encompass IM 4-6, with IM 7 making up the advanced NYHA class IIIb patient. There are no clinical trials directly comparing medical therapy with LVADs in the IM 4-7 group. However, data can be mined from the literature that can support implant of LVADs in this patient population.

#### WHAT IS THE ONE- AND TWO-YEAR SURVIVAL OF THE CHF PATIENT WITH NYHA III SYMPTOMS?

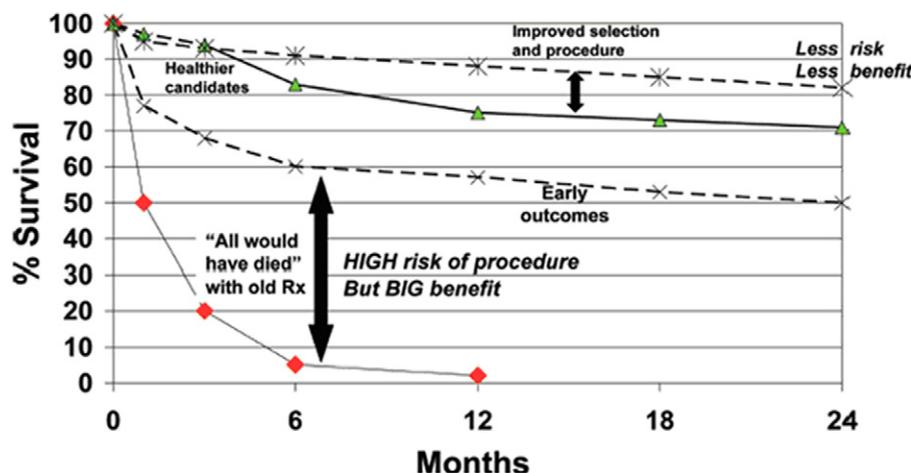
Multiple trials of medical therapy and resynchronization pacing have shown 80% and 75% survival

at 1 and 2 years, respectively. That should be the target for LVAD therapy.<sup>2</sup> Multiple studies have also shown an improvement in functional capacity and quality of life in patients with LVADs over medical therapy.<sup>3</sup> It could then be imputed that it would be beneficial to implant LVADs if the survival could match that of the medically treated patient.

Rogers et al<sup>4</sup> looked at the survival in the total cohort of patients enrolled in the HeartMate II destination trial for which 160 of 567 patients were enrolled as NYHA IIIb status. Although these class IIIb patients were sicker than the normal class IIIb patient (ie, 68% were on inotropes, 10% had intra-aortic balloon pump, and the 1- and 2-year survival was 78% and 66%, respectively). These survival outcomes are very favorable for the target class III patients. These data were used by the Food and Drug Administration to approve the HeartMate II for NYHA class IIIb patients.

Boyle et al<sup>5</sup> presented data from 101 patients at 3 busy clinical LVAD sites. Patients were stratified into three IM groups. Group 3 patients (IM 4-7) made up about one-quarter of the patient studies. They had a 95.8% 2-year survival with a short 17-day postimplant length of stay. This handily surpassed the projected 75% two-year survival target for the NYHA class III patient. Two-year survival for INTERMACS profile 1 was 51.1% and for profile 23 was 68.8%. These data demonstrate that implanting before clinical deterioration affords long-term benefits in survival.

A third study by Eckman et al<sup>6</sup> compared 89 consecutive patients implanted with IM 4-6 profile with their predicted Seattle Heart Failure Model survival. The survival in the LVAD arm was 85% and 80%, respectively, at 1 and 2 years. This was statistically superior to the Seattle Heart Failure Model predicted



**Figure 1.** Curve of downward shifting risks. Rx, prescription. (Color version of figure is available online at <http://www.semthorcardiovasc.org>.)

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survival, with an absolute 27% reduction in mortality at 2 years.

The current use of LVADs follows the curve of downshifting risks as originally described for transplantation (Fig. 1).<sup>2</sup> Initial experimentation is justified only for patients facing imminent death. As successful procedures are transplanted into less desperate settings, outcomes improve further, but the net benefit for the patient is less dramatic because the natural history is also more favorable. Hence, it is easy to make the decision to place LVADs in the IM 1-3 patient. However,

despite regulatory approval and several clinical studies that favor implantation in less sick patients, it remains a difficult decision to implant in the IM 4-7 group. The risks of the LVAD are less, but the net benefit is mitigated as well. The decision to implant in this patient population will be helped if a randomized clinical trial such as Randomized Evaluation of VAD InterVENTion before Inotropic Therapy (REVIVE-IT) can demonstrate benefit for LVAD implantation and when less invasive devices or completely implantable devices can be developed for routine and safe support.

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