Journal of the American Heart Association

EDITORIAL

Need for Unstructured Preimplantation Data to Predict Myocardial Recovery in Patients With a Left Ventricular Assist Device

Indranee Rajapreyar, MD; Thierry H. Le Jemtel, MD

The primary aim of long-term β-adrenergic blockade and renin-angiotensin-aldosterone system inhibition is reversal of left ventricular (LV) remodeling in heart failure with reduced ejection fraction (HFrEF) leading to partial or complete recovery.[1] Mechanical support with an LV assist device initially aimed to improve LV systolic performance and reversal of end-organ dysfunction in patients with advanced heart failure who were awaiting cardiac transplantation (CT) or resolution of precipitating events such as myocardial ischemia, arrhythmias, sepsis, or adverse effects of chemotherapy.[2] However, because of technical advances in pump design and former United Network for Organ Sharing (UNOS) heart allocation deficiencies, continuous-flow LV assist devices (cfLVADs) were implanted in the framework of bridge to transplant, bridge to recovery, or destination therapy with recovery of myocardial function being reported in a minority of patients. Of note, the recent change in UNOS heart allocation is associated with fewer implantations of a cfLVAD as bridge to transplant except in patients with high body mass index or comorbidities who are ineligible for CT.[3]

See Article by Maukel et al.

In this issue of the *Journal of the American Heart Association* (*JAHA*), Maukel and colleagues[4] reviewed the INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) database for sex differences in clinical outcomes. From 2006 to 2017, 6771 men and 1690 women underwent cfLVAD implantation in the framework of destination therapy. Clinical outcomes of interest were cfLVAD explant for recovery or replacement because of device complications, death, or CT. Maukel and colleagues also examined the role of sex differences in preimplant clinical, demographic, and psychosocial factors on clinical outcomes. Baseline clinical characteristics differed in women and men. Women were younger, recently diagnosed with dilated cardiomyopathy, non-White, unmarried, and had a significantly lower incidence of substance abuse and a higher incidence of severe depression than men. Myocardial recovery and cfLVAD explant were 2.5 times more likely in women than men. In women, the incidence of myocardial recovery was 2% at 1 year and 5% at 3 years in women. In men, it was 1% at 1 year and 2% at 3 years. Regardless of demographic and psychosocial characteristics, women experienced significantly more device complications requiring replacement than men.[4]

As previously noted, steady improvement in myocardial function may lead to successful LV assist device explant and myocardial remission in young women with dilated cardiomyopathy and short duration of symptoms.[1,5,6] Sex-specific causes of HFrEF such as peripartum cardiomyopathy and chemotherapy-induced cardiomyopathy for breast cancer may enhance the rate of myocardial function recovery in

Key Words: Editorials ■ sex differences ■ INTERMACS ■ left ventricular assist device ■ outcomes

Correspondence to: Thierry H. Le Jemtel, MD, 1430 Tulane Avenue, New Orleans, LA 70112. E-mail: lejemtel@tulane.edu
For Disclosures, see page 3.

JAHA is available at: www.ahajournals.org/journal/jaha

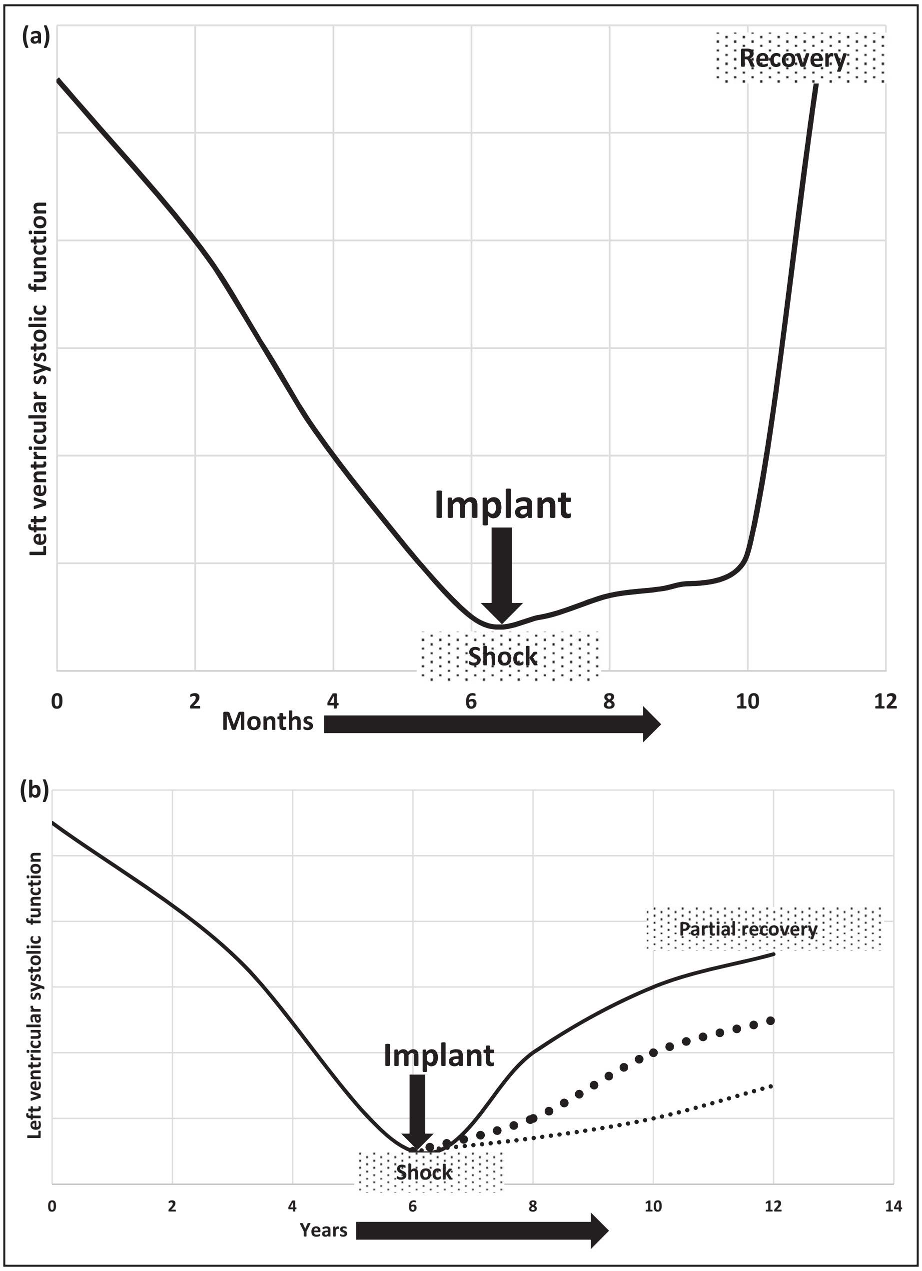

Figure 1. Myocardial recovery with remission (A) and partial myocardial recovery after continuous-flow left ventricular (LV) assist device (cfLVAD) (B).
A, Recovery of LV systolic function after cfLVAD implantation mostly results from resolution of the underlying disease in young patients, predominantly women with rapid deterioration of LV systolic function, short duration of symptoms, and moderate to severe LV dilatation. However, the cfLVAD allows adequate end-organ perfusion pending resolution of the underlying disease. **B**, The majority of elderly patients with advanced ischemic or dilated cardiomyopathy and years of symptomatic deterioration despite adherence to medical regimens and diet experience none or modest improvement in LV systolic function after cfLVAD implantation, and device removal or decommission is not considered. Even when present, LV systolic function improvement may not be sufficient for successful device removal or decommission because of the risk of LV systolic function decline after discontinuation of mechanical support.

women. Recovery of myocardial function after cfLVAD implantation was reported in single-center studies and in pooled data. Rates of myocardial function recovery after cfLVAD range from 50% to 60% in single-center studies and from 1.3% to 5% in the INTERMACS registry, HeartMate II trials, and the UNOS analysis.[5] Female sex, young age, nonischemic cause of HFrEF, absence of thoracotomy, normal renal function, and shorter duration of HFrEF were associated with recovery of myocardial function after LV assist device implantation.[1,5]

Patients who experience recovery of myocardial function while receiving medical therapy for HFrEF and after cfLVAD implantation have the same clinical profile.[5] They are young, have a dilated cardiomyopathy, and only experience symptoms and reduced functional capacity for a few months (Figure – Panel A). In contrast, patients with advanced ischemic or long-standing dilated cardiomyopathy with biventricular failure and worsening symptoms despite adherence to HFrEF pharmacotherapy and diet are unlikely to experience sufficient recovery of myocardial function for cfLVAD explant (Figure – Panel B). Long-term cfLVAD support combined with sympathetic nervous system and renin-angiotensin-aldosterone system blockade/inhibition may partially reverse myocyte and extracellular alterations and not allow return to normal LV systolic function.[5] Whether reversal of myocardial structural alterations during long-term cfLVAD therapy translate to sustained recovery of myocardial function after device explant is uncertain.

Because of increased durability and a favorable adverse effect profile, the only currently implanted cfLVAD is HeartMate III, a magnetically levitated centrifugal pump.[7] However, studies of myocardial function recovery have been performed with axial flow pumps and hydrodynamically levitated centrifugal pumps. Axial flow pumps resulted in significant improvement in LV ejection fraction compared with hydrodynamically levitated centrifugal pumps.[8] In the present study, 96% of patients in INTERMACS underwent implantation of axial flow pumps. The incidence of myocardial function recovery with HeartMate III has not been studied.

Last, sex differences in psychosocial data did not contribute to women's adverse events in the present study with the caveat that detailed psychosocial data are commonly missing in INTERMACS. A recent INTERMACS analysis, however, found psychosocial risk factors such as alcohol use, psychiatric disease, current tobacco use, and limited social support to be predictors of myocardial function recovery.[9] Patients with psychosocial risk factors who undergo cfLVAD implantation as destination therapy may experience cfLVAD-related complications that reduce access to CT.[10] Registry studies may not reliably report detailed psychosocial evaluations and reporting of psychosocial data may highly vary from center to center. The reasons for slightly higher rates of cfLVAD replacement is unclear in the analysis by Maukel et al.

In summary, the nature and staging of the underlying disease process and timing of implantation appear to be the most potent determinants of myocardial function recovery and remission after cfLVAD implantation. Unstructured data on the nature and progression of the underlying disease process are critical to develop a complete understanding of the myocardial function recovery phenomenon after cfLVAD implantation.[9] Recent changes in UNOS heart allocation may not allow young women with peripartum cardiomyopathy or patients with myocarditis to experience cfLVAD-mediated recovery of myocardial function as they promptly undergo CT.

ARTICLE INFORMATION

Affiliations

Division of Cardiology, Jefferson Heart Institute, Sidney Kimmel School of Medicine, Thomas Jefferson University, Philadelphia, PA (I.R.); and Section of Cardiology, John W. Deming Department of Medicine, Tulane University, New Orleans, LA (T.H.L.J.).

Disclosures

None.

REFERENCES

1. Jaiswal A, Le Jemtel TH, Samson R, Mancini D. Sustained cardiac recovery hinges on timing and natural history of underlying condition. *Am J Med Sci*. 2018;356:47–55. doi: 10.1016/j.amjms.2018.02.008
2. Han JJ, Acker MA, Alturi P. Left ventricular assist devices. *Circulation*. 2018;138:2841–2851. doi: 10.1161/CIRCULATIONAHA.118.035566
3. Mullan CW, Chouairi F, Sen S, Mori M, Clark KAA, Reinhardt SW, Miller PE, Fuery MA, Jacoby D, Maulion C, et al. Changes in use of left ventricular assist devices as bridge to transplantation with new heart allocation policy. *JACC Heart Fail*. 2021;9:420–429. doi: 10.1016/j.jchf.2021.01.010
4. Maukel LM, Weidner G, Beyersmann J, Spaderna H. Sex differences in recovery and device replacement after left ventricular assist device implantation as destination therapy. *J Am Heart Assoc*. 2022;11:e023294. doi: 10.1161/JAHA.121.023294
5. Burkhoff D, Topkara VK, Sayer G, Uriel N. Reverse remodeling with left ventricular assist devices. *Circ Res*. 2021;128:1594–1612. doi: 10.1161/CIRCRESAHA.121.318160
6. Shah P, Psotka M, Taleb I, Alharethi R, Shams MA, Wever-Pinzon O, Yin M, Latta F, Stehlik J, Fang JC, et al. Framework to classify reverse cardiac remodeling with mechanical circulatory support: the Utah-Inova stages. *Circ Heart Fail*. 2021;14:e007991. doi: 10.1161/CIRCHEARTFAILURE.120.007991
7. Mehra MR, Uriel N, Naka Y, Cleveland JC, Yuzefpolskaya M, Salerno CT, Walsh MN, Milano CA, Patel CB, Hutchins SW, et al. A fully magnetically levitated left ventricular assist device- final report. *N Engl J Med*. 2019;380:1618–1627. doi: 10.1056/NEJMoa1900486
8. Al-Sarie M, Rauf A, Kfoury AG, Catino A, Wever-Pinzon J, Bonios M, Horne B, Diakos N, Wever-Pinzon O, McKellar S, et al. Myocardial structural and functional response after long-term mechanical unloading with continuous flow left ventricular assist device: axial versus centrifugal flow. *JACC Heart Fail*. 2016;4:570–576. doi: 10.1016/j.jchf.2016.02.015
9. Topkara VK, Elias P, Jain R, Sayer G, Burkhoff D, Uriel N. Machine learning-based prediction of myocardial recovery in patients with left ventricular assist device support. *Circ Heart Fail*. 2022;15:e008711. doi: 10.1161/CIRCHEARTFAILURE.121.008711
10. DeFilippis EM, Breathett K, Donald EM, Nakagawa S, Takeda K, Takayama H, Truby LK, Sayer G, Colombo PC, Yuzefpolskaya M, et al. Psychosocial risk and its association with outcomes in continuous-flow left ventricular assist device patients. *Circ Heart Fail*. 2020;13:e006910. doi: 10.1161/CIRCHEARTFAILURE.120.006910