

Left ventricular assist devices in end-stage heart failure with “fixed” pulmonary hypertension—a test of reversibility?

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Pulmonary hypertension (PH) secondary to left heart disease is one of the risk factors for morbidity and mortality after orthotopic heart transplantation. In cardiac allograft recipients PH can lead to acute right ventricular failure resulting in high mortality rates. When longstanding PH becomes refractory to medical treatment, it is considered “fixed”; at this stage vasodilator challenges do not produce any decrease in pulmonary artery pressures or the calculated pulmonary vascular resistance. Mixed PH is also called PH out-of-proportion to left-sided filling pressures and consists of increased left-sided filling pressures in addition to elevated pulmonary vascular resistance. Mixed PH that is responsive to vasodilator challenge is called reversible / reactive or vasoreactive PH, but mixed PH that is not reversible is called irreversible or fixed or refractory or persistent PH.¹ Fixed PH (>2.5 Wood units) is an absolute contraindication to cardiac transplantation due to its detrimental effects on the right ventricular function.²⁻⁵ When pharmacological agents fail to decrease left ventricular filling pressures chronically, mechanical unloading becomes necessary to reverse the PH due to left heart disease. Unloading the left ventricle with a left ventricular assist device (LVAD) progressively decreases pulmonary vascular resistance to normal values in patients making them eligible for heart transplantation. Contraindications for LVAD implant include active infection/malignancy or end stage renal disease at the time of implant.⁶

In a small study of ten patients with severe pulmonary hypertension refractory to medical treatment, continuous flow mechanical support was provided as a bridge to transplant. Pulmonary artery pressures, transpulmonary gradients, and

pulmonary vascular resistance were all significantly decreased after 1-6 months of LVAD support, suggesting that medically unresponsive PH can be reversed by mechanical unloading of the LV.⁷ This approach has increased survival in patients whose fixed PH was reversed prior to transplantation.⁷ LVAD therapy is also applicable to patients with RV failure secondary to LV failure.⁸ Therefore, the use of LVADs as a bridge to cardiac transplantation has gained momentum and importance in this patient population.⁷⁻¹⁰ Table 1 shows the outcomes in small studies using LVADs to reverse PH secondary to left heart disease. Factors that actively determine reversibility of PH due to left heart disease are not clear in the existing literature. Hence, no selection criteria can be currently used in these patients except for the fact that they have PH refractory to medical therapy.

Another interesting aspect of LVAD support in reversing secondary PH is the role of continuous flow (CF) pumps versus pulsatile pumps.⁴ In a small single center study of 27 LVAD patients (15 with CF pumps [Heart Ware Inc., Framingham, MA] and 12 with pulsatile pumps [Berlin Heart EXCOR, Berlin, Germany]), the patients with CF pumps had greater reductions in pulmonary artery systolic pressures. No significant differences were noted in right ventricular systolic motion, tricuspid annular plane systolic excursion, and right ventricular ejection fraction.⁴ In another single center prospective study, 29 patients with centrifugal pumps had significant improvement in their transpulmonary gradients, pulmonary artery systolic pressures, mean pulmonary artery pressures, and pulmonary vascular resistance. These differences developed within one month post implantation. Patients bridged with centrifugal CF pumps had post-transplant survival comparable to those who were transplanted directly.¹¹ The improved reduction in pulmonary artery systolic pressures in patients managed with CF pumps has been attributed to the fact that CF pumps unload the

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DOI: 10.12746/swrccc2016.0416.213

ventricle throughout the entire cardiac cycle.⁴ These small studies require validation with randomized clinical trials to establish scientific proof.

Adjunct medical therapies, such as the addition of phosphodiesterase inhibitors and endothelin receptor blockers, have also shown additional benefits in reducing secondary PH.^{12,13} In a small study of eight LVAD patients who were difficult to wean off inhaled nitric oxide and inotropic support post-LVAD implantation, sildenafil significantly reduced pulmonary artery systolic pressures in about 90 minutes and allowed weaning of these agents.¹² In a single center retrospective analysis of 40 LVAD patients, secondary PH was reduced by 1.4 Wood units after six months as compared to baseline with bosentan.¹³ Table 2 lists the few studies reporting drug effects.

In summary, the evolution of mechanical circulatory support with durable LVADs has made it possible to transition patients with PH secondary to left heart failure to another level of care. If they have reversible PH, they can become transplantation candidates; if their PH is irreversible, they can continue to receive LVAD support for life. Figure 1 summarizes this approach in the management of secondary fixed PH. Although larger studies and randomized trials are needed to define the utility of LVADs as a test of reversibility, this approach has had increased use in end-stage heart failure patients undergoing complex care.

Key words-editorial, pulmonary hypertension, heart assist devices, cardiac transplantation

Figure 1 LVADS in the management of "fixed" PH in end-stage heart failure

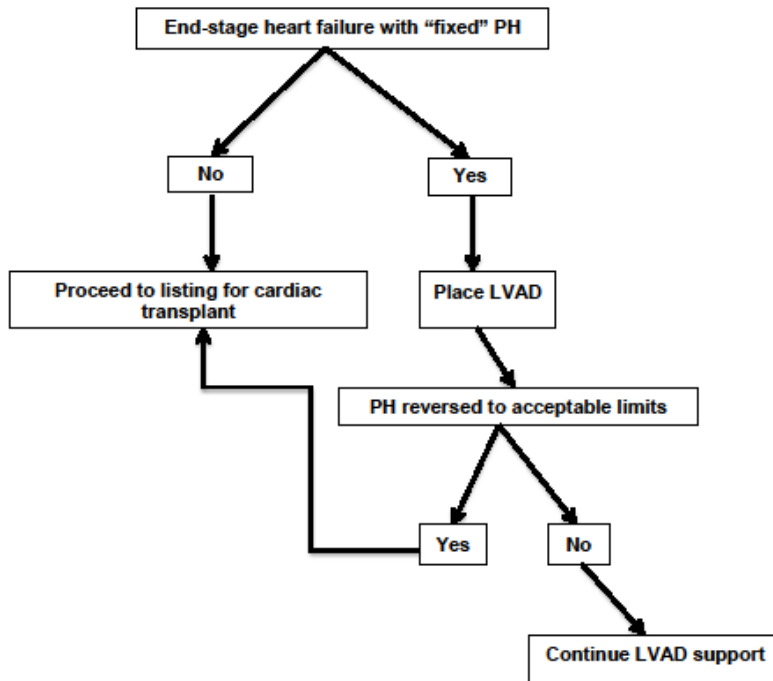


Table 1 : Use of LVADS to decrease fixed PH due to left heart disease

Study type	n	LVAD type	Baseline PVR	Post-implant PVR	Duration of LVAD support	Conclusions	Reference
Case report	1	HMII	6.6*	2.8	10 weeks	Post-transplant pulmonary hemodynamics were normal at 1 year	14
Case series	6	TCIHM=4 Novacor=1 Jarvik=1	5.7 ± 0.7	2.0 ± 1.2	191 ± 86 days	All patients survived to transplant 5/6 were alive at 16.2 ± 10.5 months	15
Observational study	29	Heartware=8 Ventra assist=21	5.0 ± 1.5	2.1 ± 0.5	30 - 90 days	Patients bridged to candidacy have post-transplant survival comparable with those with normal PVR	11
Observational study	78	MicromedDebakey DuraHeart Novacor	5.1 ± 2.8	2.0 ± 0.9	3 years	Comparable survival in patients with and without PH corrected with LVADS	16

PVR-pulmonary vascular resistance, * Wood units

Table 2 : Concomitant use of pharmacological agents in LVAD patients to reduce PH

Study type	n	Pharmacological agent	Conclusions	Reference
Retrospective	10	Sildenafil	All patients were weaned off inotropes and inhaled NO with further reduction in PH after LVAD implant	12
Open label clinical trial	138	Sildenafil	Sildenafil significantly decreased the PVR in patients on LVAD in 12 to 15 weeks post-implant as compared to controls with only LVADS	17
Observational study	50	Bosentan	Bosentan treated patients showed a decrease in PVR as compared to baseline at 6 month follow up	13

NO- nitric oxide, PH-pulmonary hypertension, PVR-pulmonary vascular resistance, LVAD-left ventricular assist device

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Details

1. Submitted-8/29/2016
2. Accepted-10/13/2016/2016
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6. Conflicts of interest-none