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Hemodynamic Aberrancies in Left Ventricular Assist Device–Associated Heart Failure Syndromes

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The advent of the fully magnetically levitated HeartMate 3 left ventricular assist device (LVAD) has enabled a marked reduction in hemocompatibility-related adverse events, with a near-elimination of pump thrombosis, and a marked decrease in stroke in LVAD recipients.[1,2] As a result, a survival benchmark for LVAD therapy has been established—prolongation of the median survival of more than 5 years in patients with advanced heart failure with otherwise severely limited 1-year survival.[3]

Even as we mark this success, our attention must shift toward residual risk reduction with contemporary use of LVAD therapy. The foremost reason for rehospitalizations and death during support, is a consequence of heart failure syndromes (HFS): a constellation of signs and symptoms reflective of congestion and/or low output.[4,5] Because the right ventricle remains unsupported with LVAD therapy and often worsens in function because of early hemodynamic and inflammatory stress, we have generally assumed that most heart failure events reflect right heart failure, perhaps a sweeping oversimplification. Such a broad attribution is unwise and likely deviates attention away from other remediable causes of HFS. We believe that the systematic clinical phenotyping of HFS must be undertaken, one that is directed on the detection of specific patterns of hemodynamic aberrancy (HDA) that identify the primary origination of the deficit resulting in the HFS. Therefore, we propose a phenotypical classification of HFS and their accompanying HDAs, as illustrated in Fig. 1.

As depicted in Fig. 1, HDAs should be divided into 4 distinct compartments including (a) right-side dominant, (b) left-side dominant, (c) pump abnormality dominant, and (d) extracardiac aberrancies. Although multiple etiologies may be in play within a patient, it is important to identify the primary deficit and then to further elucidate secondary contributors. Right-side dominant HDAs are further divided into abnormalities of right ventricular (RV) preload, afterload, and contractile insufficiency. RV contractile insufficiency may be due to primary myocardial dysfunction or ventricular arrhythmias, or secondary to the impact of the pump on septal dynamics and RV geometry (which may be a result of excessive LVAD associated unloading of the left ventricle). The physiologic consequence of all right-side dominant HDAs is a decrease of the available preload to the LVAD. Left-side dominant HDAs include inadequate optimization of LVAD pump flow (usually manifest with significant mitral regurgitation and dilation of the left ventricular chamber) and the presence of a recirculation syndrome in the setting of aortic regurgitation. The physiological consequence of all left-side dominant HDAs is elevation of post-capillary pulmonary pressures. Pump abnormality–dominant HDAs include an obstruction to flow within the inflow or outflow graft and an increase in afterload to the pump in the setting of systemic hypertension. The physiologic consequence of all pump abnormality dominant HDAs is a

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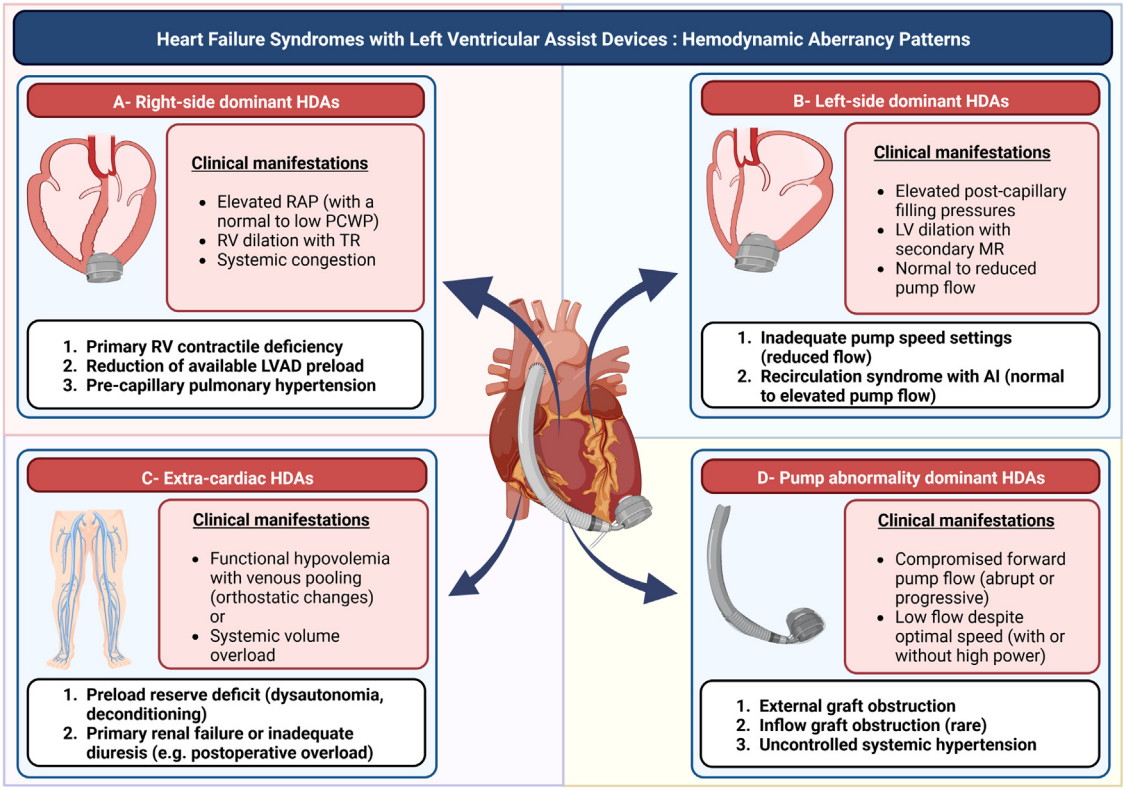

Fig. 1. The pathophysiological hallmark of right-sided HDAs is to decrease the preload available to the LVAD to ensure adequate systemic flow. Classically, this manifests with increased right-sided filling pressures and a relatively smaller LV cavity size. In contrast, recirculation syndrome owing to aortic valve regurgitation does not show low pump flow, but results in a dilated LV chamber and elevated left-sided filling pressures with poor systemic perfusion state. The LVAD interrogation overestimates the flows in this situation. Alternatively, secondary mitral regurgitation is associated with an increased LV dilation and elevated pulmonary filling pressures which requires higher speed settings to optimize cardiac pressures. The diagnosis of outflow graft obstruction via kinking, bending, or gelatinous obstruction requires the use of contrast-assisted imaging with computed tomography scanning, often with 3-dimensional reconstruction for accurate diagnosis. Hypertension should be carefully evaluated, and orthostatic pressures ascertained to ensure that attempts to treat supine blood pressure do not inadvertently result in orthostatic hypotension. This can be a problem in patients with autonomic dysfunction and is further affected by ventricular–vascular uncoupling owing to the presence of the LVAD. Venous capacitance issues can be difficult to diagnose, because they do not classically present as congestive states, but instead mimic a cold and dry physiology owing to preload insufficiency and consequent low pump flows, particularly upon ambulation. In some instances, renal insufficiency could create a hypervolemia in the setting of optimal pump function or in more acute circumstances (usually early perioperative events) pericardial effusion or tamponade could be a contributor to extracardiac effects. AI, aortic insufficiency; HDA, hemodynamic aberrancy; LV, left ventricle; LVAD, left ventricular assist device; MR, mitral regurgitation; PCWP, pulmonary capillary wedge pressure; RAP, right atrial pressure; RV, right ventricle.

compromise to adequate forward flow despite an appropriately set pump speed. Finally, extracardiac HDAs are due to functional hypovolemia owing to preload reserve deficit, with venous pooling or mechanisms that decrease the ability to provide an adequate preload to the right ventricle. Although this particular entity may resemble hypovolemia, it results in low-flow states, especially during ambulation, whereas filling pressures in supine posture may seem to be normal. Hypervolemia in the setting of inadequate diuresis (as with postoperative volume overload) or renal insufficiency may also result in a HFS owing to extracardiac causes.

The typical presentation of HFS involves signs and symptoms related to congestion and/or low LVAD flows (which may develop gradually) with frequent pulsatility index–related events on LVAD interrogation and consequent systemic hypoperfusion. Because the various phenotypes of HDAs have largely similar clinical manifestations, it is important to approach clinical phenotyping carefully and not assume an etiology in the absence of a systematic approach. This point is important, because accurate phenotyping will allow constructive identification of corrective options. As an example, recirculation syndrome may be dealt with by aortic valve repair (using percutaneous or minimally invasive surgical techniques), or inadequate unloading (with an adequate preload) will require increased LVAD speed adjustments to enhance systemic perfusion and hemodynamics. Venous insufficiency may require attention on ensuring ambulatory preload through calf

conditioning exercises or the use of therapy to increase vascular tone. Similarly, pump factors could be treated with surgery in the case of outflow graft obstruction, or simply by better blood pressure control.

Significant overlap amongst the HDA compartments exists in the clinical setting. For example, significant mitral regurgitation owing to insufficient LVAD unloading will result in post-capillary pulmonary hypertension, which may precipitate RV failure. However, systematic identification of this clinical scenario as a left-side dominant HDA through the integration of echocardiography, hemodynamic evaluation, device interrogation, and the bedside physical examination, would enable appropriate categorization of the HFS and identification of treatment opportunities. We do recognize that multiple components may coexist in some patients; therefore, it may be wise to subcategorize a primary HDA and coexisting secondary HDAs that comprise the HFS.

We anticipate that a phenotype-based classification system of HDAs in LVAD-associated HFS will decrease misclassifications, better identifying and quantifying the prevalence of these various abnormalities while allowing for the evaluation of the effectiveness of management strategies. Additionally, more accurate phenotyping will allow us to better understand the complex interactions, competing risks of such HDAs among each other and their contributions, particularly within the context of clinical studies that report these outcomes. In doing so, we believe that the burden of heart failure–related readmissions and their associated mortality will decrease, allowing patients with LVAD therapy to live even longer and better lives.

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