Hemodynamic Aberrancies in Left Ventricular Assist Device Associated Heart Failure Syndromes

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PII: S1071-9164(22)00722-9
DOI: https://doi.org/10.1016/j.cardfail.2022.09.007
Reference: YJCAF 5103

To appear in: Journal of Cardiac Failure

Received date: 31 August 2022
Revised date: 21 September 2022
Accepted date: 21 September 2022

Please cite this article as: Jacinthe Boulet MD CM, MPH, Aditi Nayak MD, MS, Mandeep R. Mehra MD, MSc, FRCP, Hemodynamic Aberrancies in Left Ventricular Assist Device Associated Heart Failure Syndromes, Journal of Cardiac Failure (2022), doi: https://doi.org/10.1016/j.cardfail.2022.09.007

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Acknowledgements

Disclosures

Dr. Boulet has no disclosures to report. Dr. Nayak has no disclosures to report. Dr. Mehra reports payments made to his institution from Abbott for consulting, consulting fees from Janssen, Mesoblast, Broadview Ventures, Natera, Paragonix, Moderna and Baim Institute for Clinical Research; he is a scientific advisory board member for NuPulseCV, Leviticus, Transmedics and FineHeart.

Word count: 891
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The advent of the fully magnetically levitated HeartMate 3 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. As a result, a survival benchmark for LVAD therapy has been established – prolongation of median survival more than 5-years, in patients with advanced heart failure with otherwise severely limited 1-year survival. Even as we mark this success, our attention must shift towards residual risk reduction with contemporary use of LVAD therapy. The foremost reason for re-hospitalizations 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. Since 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 broad attribution is unwise and likely deviates attention away from other remediable causes of HFS. We believe that systematic clinical phenotyping of HFS must be undertaken, one that is directed on 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 Figure 1.

As depicted in Figure 1, HDAs should be divided into 4 distinct compartments including a) right-side dominant, b) left-side dominant, c) pump abnormality dominant, and d) extra-cardiac aberrancies. While 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, 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 reduction of 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 presence of a recirculation syndrome in the setting of aortic regurgitation. The physiologic 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 increase in afterload to the pump in the setting of systemic hypertension. The physiologic consequence of all pump abnormality dominant HDAs is a compromise to adequate forward flow despite an appropriately set pump speed. Finally, *extra-cardiac HDAs* are due to “functional” hypovolemia due to preload reserve deficit, with venous pooling or mechanisms that reduce ability to provide an adequate pre-load to the right ventricle. Although this particular entity may resemble hypovolemia, it results in low flow states especially during ambulation, while filling pressures in supine posture may appear normal. Hypervolemia in the setting of inadequate diuresis (as with post operative volume overload) or renal insufficiency may also result in a HFS due to extracardiac causes.

The typical presentation of HFS involves signs and symptoms related to congestion and/or low LVAD flows (that may develop gradually) with frequent pulsatility index related events on LVAD interrogation and consequent systemic hypoperfusion. Since 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 is important since 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 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 will exist in the clinical setting. For example, significant mitral regurgitation due to insufficient LVAD unloading will result in post-capillary pulmonary hypertension, which may precipitate right ventricular failure. However, systematic identification of this clinical scenario as a left side dominant HDA through integration of echocardiography, hemodynamic evaluation, device interrogation and the bedside physical
exam, would enable appropriate categorization of the HFS and identification of treatment opportunities. We do recognize that multiple components may co-exist in some patients and therefore it may be wise to subcategorize a primary HDA and co-existing secondary HDAs that comprise the HFS.

We anticipate that a phenotype-based classification system of HDA’s in LVAD associated HFS will decrease misclassifications, better identify, and quantify the prevalence of these various abnormalities while allowing for evaluation of 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.

References

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Figure Legend

**Figure 1.** AI: aortic insufficiency, HDA: hemodynamic aberrancy, LV: left ventricle, LVAD: left ventricular assist device, MR: mitral regurgitation, RAP: right atrial pressure, PCWP: pulmonary capillary wedge pressure, RV: right ventricle. The pathophysiological hallmark of a Right-Sided HDAs is to reduce 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 due 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 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 use of contrast assisted imaging with computerized tomography, 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 due to the presence of the LVAD. Venous capacitance issues can be difficult to diagnose since they do not classically present as congestive states but instead mimic a cold and dry physiology due 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.