

EDITORIAL COMMENT

# 3D Echocardiography and Ventricular Unloading With Continuous Flow LVAD

## Potential Advantages to Optimize Patient Outcome\*

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Continuous-flow left ventricular assist devices (CF-LVADs), the Heartmate II (HMII) (St. Jude Medical, Pleasanton, California) and HVAD (HeartWare International, Framingham, Massachusetts), have significantly improved survival, quality of life, and functional capacity in patients with end-stage heart failure (1). These observed benefits are influenced by the ability of the LVAD to reduce elevated left ventricular (LV) filling pressure and augment systemic cardiac output. The degree of LV unloading is influenced by afterload and pre-load and the set pump speed (determined by the LVAD team). There are also unique differences between the available pumps that may influence the degree of LV unloading for an individual patient.

A primary objective when adjusting LVAD pump speed is to unload the LV and improve systemic blood flow to clinically improve shortness of breath and fatigue, and associated end-organ dysfunction. HMII and HVAD pump speed selection should avoid inadequate LV unloading to minimize the risk of insufficient circulatory support and smoldering decompensated heart failure. An equally important goal is to avoid excessive LV unloading as seen at high speeds to minimize adverse effects such as LV suction events and interventricular septal bowing into the LV with associated compromise of right ventricle (RV) function and/or increased tricuspid regurgitation (2).

In this issue of *iJACC*, Addetia et al. (3) reported a hemodynamic and 3-dimensional (3D) echocardiographic examination of 31 patients (19 with HMII and 12 with HVAD) referred for a clinically indicated ramp test with right heart catheterization for LVAD speed adjustments. The primary aim of the study was to determine how device speed influences ventricular morphology, including septal geometry, with a focus to test the feasibility of a 3D echocardiography examination during ramp testing. The examined topic and the observations made are extremely important for 2 primary reasons.

SEE PAGE 159

First, there is a paucity of data that define a difference in ventricular unloading based on LV and RV morphology between the 2 available pumps that may have important clinical implications. The HMII is an axial flow pump, extrathoracic in location (placed below the diaphragm), and characterized by propelled blood from the LV into the pump parallel to the axis of the rotor. By contrast, the HVAD is a centrifugal pump, intrathoracic (pericardial placement), with blood propelled from the LV through the rotor pump with blood exiting at a 90° angle (perpendicular as opposed to parallel). It is important to highlight that, based on a previous study and as illustrated in this examination, at typical operating pump speeds, the degree of LV unloading as detected by measured hemodynamics is felt to be similar between the HMII and HVAD (4). In addition, based on the ENDURANCE trial (A Clinical Trial to Evaluate the HeartWare® Ventricular Assist System) (the only prospective, randomized study designed to compare safety and efficacy of the HVAD and HMII as destination therapy), there were no significant differences in outcomes related to the degree of LV unloading induced by these 2 different pumps (5). Specifically, survival free from disabling stroke, New York Heart Association functional class, quality of life, and exercise

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capacity at 2 years were similar between the HVAD and HMII. However, for individual patients, a better understanding of the dynamic LV, RV, and interventricular septal response with pump speed augmentation is needed to best detect early excessive LV unloading to potentially minimize adverse effects including bowing of the interventricular septum into the LV and possibly worsening RV failure, a long-term consequence that is becoming increasingly recognized (6).

Second, although 2D echocardiography has proven to be very useful to track ventricular size and function during LVAD support, an established limitation is difficulty in accurately measuring LV volumes using standard apical views due to the apical inflow cannula and associated shadowing or attenuation artifact (7). The adequacy of LV unloading is typically determined by invasively measured hemodynamics and/or with echocardiography at baseline and with increased pump speeds (ramp testing). 2D echocardiography with color and spectral Doppler specifically helps to understand LV chamber size reduction, interventricular septal positioning, mitral valve regurgitation severity, and estimated LV filling pressure (8,9). 3D echocardiography is intriguing as a modality to monitor patients supported by CF-LVADs because it permits the acquisition of full-volume datasets to allow real-time imaging, requires no geometric assumptions, and prevents foreshortening of the LV cavity to permit analysis of regional myocardial function, including dynamic changes of the interventricular septum (10).

There are 2 main findings in the paper published in this issue of *iJACC*. First, in patients supported by the HMII, LV volumes progressively and significantly decreased (mean decrease of ~127 ml;  $p < 0.01$ , with  $\geq 20\%$  reduction in  $>80\%$  of the patients) due to the LV walls moving toward the center with significant shortening of the base-to-apex dimension. These changes based on 3D datasets defined the LV becoming more conical and less spherical at the highest versus the lowest pump speed tested. Although the averaged RV volumes in patients supported by the HMII initially remained stable, at higher pump speeds (e.g.,  $>10,000$  revolutions/min), RV volumes subsequently increased along with interventricular septal bulging into the LV as reflected by the measured RV septal curvature ( $0.97 + 0.11$  at lowest vs.  $1.03 + 0.10$  at highest speed;  $p = 0.07$ ).

Second, in patients supported by the HVAD, the reduction in 3D derived LV volumes were much less pronounced (mean decrease of ~51 ml), and there was no discernable change in either the LV global

sphericity and conicity indices nor in RV septal and free-wall curvature measurements comparing the lowest and highest speeds (e.g.,  $>3,000$  revolutions/min). Interestingly, LV sphericity was higher for HVAD at the highest speed when compared with the HMII ( $0.71 + 0.07$  vs.  $0.62 + 0.07$ , respectively;  $p = 0.004$ ). This difference comparing the HVAD and HMII was not appreciated in the 2D LV dimension measurements made at the same speed, but were appreciated when expressing the change in LV size as a percent reduction in LV dimension using the LV dimension as the reference at the lowest pump speed (when LV size is the greatest during CF-LVAD support).

A unique aim of the study was to include 3D imaging obtained from both the LV and RV to understand the paired response, given the concern of worsening RV size and function at higher levels of support. Coupled with performing simultaneous right heart catheterization (supine positioning), feasibility was only 56%, which highlights that more work needs to be done before widespread clinical adoption of 3D echocardiography analysis to guide pump speed selection. It is reassuring that the interobserver variability was under 10% for the new reported indices LV sphericity and RV free-wall and RV septal curvature. As alluded to by the authors, it remains important to better understand 2D ventricular morphology changes with ramp testing based on linear dimensions of RV size in combination with % LV linear reduction and quantitative assessments of interventricular septum motion.

Other limitations of the study included a small sample size of patients derived from 1 center and pooling of data to compare 3D echo datasets at high versus low pump speed settings. In clinical practice, the final ramp-tested speed setting is typically not at the extreme ends of the pump speed spectrum. It remains to be determined whether these initial 3D echo observations based on LV and RV shape and size changes in response to ramp testing can be reproduced with similar accuracy at centers with varying noninvasive speed setting practices and in patients with a greater underlying spectrum of native ventricular contractility, pre-load, afterload, and inflow cannula position, all of which influence the pressure-volume relationship and ventricular morphological changes with pump speed alterations.

In the end, a goal is to better understand the differential LV, RV, and interventricular response during ramp testing in patients supported by different CF-LVADs. The ability to accurately detect LV decompression (e.g., higher pump speed) coupled with RV dilatation and interventricular septum bulging into

the LV may help to curb late RV failure and may potentially guide device selection for patients at risk of RV failure. In addition, another potential advantage with achieving the greatest tolerated LV size reduction is to enhance myocardial recovery in select patients by at least temporary minimizing wall stress, which is known to be proportional to LV size. Ultimately, further studies will be needed to define the clinical implication of using echocardiographic-guided pump

speed setting algorithms (2D and 3D) to move the field forward to best optimize outcomes in patients supported by CF-LVADs. This study marks an important step in the right direction to achieve these goals.

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