Programmed Speed Reduction Enables Aortic Valve Opening and Increased Pulsatility in the LVAD-Assisted Heart

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Aortic valve opening (AVO) during left ventricular assist device (LVAD) support aids in preventing valve fusion, incompetence, and thrombosis. The programmed low speed algorithm (PLSA) allows AVO intermittently by reducing continuous motor speed during a dwell time. AVO and hemodynamics in the LVAD-assisted heart were measured using a HeartMate II (Thoratec Corporation, Pleasanton, CA) LVAD with a PLSA controller in a mock circulatory loop. Left ventricle and aortic pressures, LVAD, and total aortic flow were measured during pre-LVAD, non-PLSA and PLSA combinations of cardiac function, and LVAD speed. The low cardiac setting corresponded to a pre-LVAD cardiac output of 2.8 L/min, stroke volume of 40 ml, and ejection fraction of 22%; the medium setting produced values of 3.5 L/min, 50 ml, and 28%, respectively. Results show that the PLSA controller set at 10 krpm, dropping to 7 krpm for dwell time of 6 s, adequately produced AVO for all tested cardiac functions with only minimal changes in cardiac output. However, AVO frequency was independent of opening area and systolic duration, which both decreased with increasing LVAD support. Furthermore, aortic pulsatility index quadrupled in the aortic root and doubled in the distal aorta during PLSA conditions, providing evidence that AVO and blood mixing are enabled by PLSA control at the appropriate speed. *ASAIO Journal* 2015; 61:540–547.

Key Words: LVAD, heart, aortic valve, mechanical circulatory assist

Aortic valve opening (AVO) during left ventricular assist device (LVAD) support is considered important for preventing valve fusion and possibly aortic incompetence (AI). However, increasing LVAD support results in a decrease or even elimination of AVO.[1] Although there is no direct evidence to support it, common clinical practice is to set the HeartMate II (HM II) (Thoratec Corporation, Pleasanton, CA) speed to encourage at least intermittent valve opening. AVO is considered to be beneficial for several reasons: first, by opening the valve, AI and possibly leaflet fusion are prevented, and second, better blood mixing between aortic root and left ventricle (LV), which reduces thrombus potential. These two classes of problems arise from the alteration in solid and fluid mechanics in the aortic valve (AV) after implantation with a continuous flow LVAD.

Aortic incompetence has emerged as a significant problem with LVAD support. Studies have found that 25–52% of continuous flow (CF)-LVAD patients develop AI within 12 months of support.[2,3] Aortic incompetence is detrimental in the LVAD patient for a number of reasons: a damaged valve has a lower chance of bridging to recovery, AI decreases exercise capacity, and the regurgitant flow creates a loop that increases blood damage by excessive exposure to the pump.[4] There is concern that AI may promote mitral regurgitation, pulmonary hypertension, and right heart failure.[5] Studies have demonstrated that patients with intermittent AVO are less likely to develop AI.[2,6,7] Thus, current practice is to start with a high level of LVAD support after the implant but to gradually decrease the LVAD speed until intermittent AVO is observed. If no negative signs are observed, the operating speed will be set at that level when the patient is discharged.

The downside of decreasing LVAD speed to promote AVO is that this may lead to deficient cardiac output for patients with LV dysfunction, and they may not receive sufficient end-organ perfusion. Furthermore, decreasing flow through the LVAD may contribute to improper washing of bearings and lead to thrombosis. One recent study reported that thromboembolism was greater in patients supported at lower speeds and more frequent AVO,[8] providing another perspective on achieving the right balance of physiology and cardiac biomechanics.

To address the need for speed control that enables AVO without compromising cardiac output and perfusion, a simple algorithm was implemented on the HM II controller called programmed low speed algorithm (PLSA). The PLSA controller allows a dwell time (DwT) to be set during which the LVAD fixed speed (FSP) drops to a lower speed (LSP) to promote AV opening. The amount (FSP–LSP), rate (RoD, rate of deceleration; RoA, rate of acceleration), and length of speed decrease (DwT) can be specified using the parameters shown in **Figure 1**. This PLSA controller was tested using a mock loop, in which hemodynamics and AVO can be measured directly for a range of HM II support conditions. Thus, the overall goal of this study was to assess the effectiveness of the PLSA controller in providing intermittent AVO. The study was designed to characterize the behavior of the HM II PLSA controller in a mock circulatory loop, to measure AVO during standard and PLSA HM II control, and to relate the hemodynamics to aortic valve biomechanics to provide guidance for clinicians.

Methods

Experimental Setup

Experimental studies were performed with the San Diego State University (SDSU) cardiac simulator (CS), a mock loop of

Submitted for consideration November 2014; accepted for publication in revised form April 2015.

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Funding for these studies was provided by Thoratec Corporation.

Disclosure: Funding provided by Thoratec Corporation as part of a Research Study Agreement, from which S. Tolpen received support. K. May-Newman is a consultant for Thoratec Corporation.

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DOI: 10.1097/MAT.0000000000000241

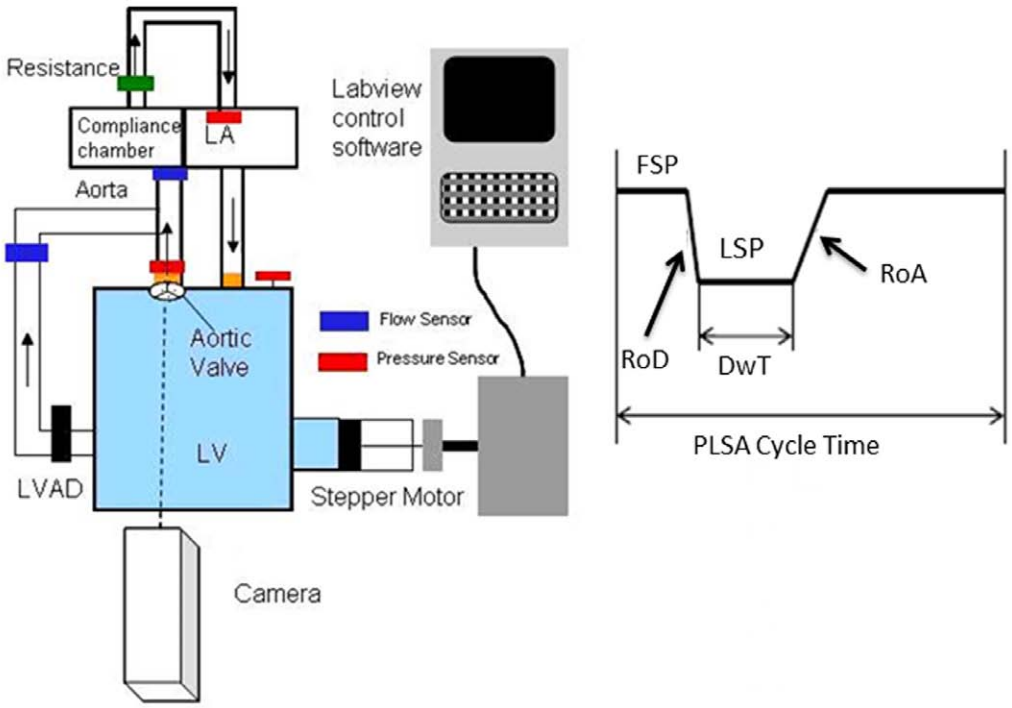

Figure 1. The San Diego State University (SDSU) cardiac simulator was configured to study aortic valve biomechanics during programmed speed reduction. The hemodynamics are measured including distal aortic and left ventricular assist device (LVAD) conduit flows, as well as left ventricle (LV) and aortic pressures. A high-speed video camera is used to measure aortic valve opening (AVO) area and time. The programmed low speed algorithm (PLSA; see inset) includes a periodic dwell time (DwT) during which the LVAD operates at a low speed (LSP) then resumes its normal fixed speed (FSP). The rate of deceleration (RoD) and rate of acceleration (RoA) can be prescribed to control the rate of speed change. full color online

the LVAD-assisted heart.[1,9] A HM II LVAD (Thoratec Inc.; Pleasanton, CA) using the PLSA controller was incorporated into the SDSU CS (**Figure 1**). LV pressure (LVP) and aortic root pressure (AoP) were recorded with Transpak IV pressure sensors (ICU Medical, San Clemente, CA). The total aortic flow and LVAD flow (LVADQ) were recorded using Transonic ME-PXL Series flow sensors (Transonic Systems, Inc., Ithaca, NY). All sensors were calibrated using a 2-point calibration technique. LabChart software (ADInstruments, Dunedin, New Zealand) was used to record data during experimentation at a frequency of 200 Hz. The simulator settings were varied over a wide range to ensure coverage of physiologic conditions.

The design of the simulator is based on a three-element Windkessel model following the methods of Yin *et al.*[10] and has been described previously.[11] The beating of the LV is simulated with a piston attached to the tank that displaces volume according to the cardiac waveform. The piston displacement can be scaled to produce different levels of function (CS). The pre-LVAD condition was simulated by clamping the LVAD conduit with the LVAD off, and adjusting the systemic resistance clamp downstream of the aorta to produce a cardiac output of 3.5 L/min at a mean AoP of 60 mm Hg (CS Med), representative of heart failure patients with a severity of New York Heart Association (NYHA) IV.[12,13] The resistance and compliance of the circuit were maintained constant for the duration of the study and heart rate maintained at 70 bpm. The experimental protocol was performed in two steps: first establishing the non-PLSA hemodynamics as a baseline, followed by measurements under several PLSA conditions. For the non-PLSA conditions, six different LVAD speeds were tested (6, 7, 8, 9, 10, and 11 krpm), at three levels of CS function: off, low, and medium (CS Off, CS Low and CS Med). The speed at which the flow pattern changed from series to parallel for each cardiac function level was established, and PLSA conditions identified for study. The following PLSA parameters were fixed: DwT at 6 s, PLSA cycle time 60 s, RoA and RoD at rates of 4 krpm/s. Ten PLSA conditions were evaluated, with the FSP and LSP noted as 8k_6k, 9k_6k, 10k_6k, 11k_6k, 9k_7k, 10k_7k, 11k_7k, 9k_8k, 10k_8k, and 11k_8k. Data (3–5 min) were acquired for each condition at a frequency of 200 Hz using LabChart (ADInstruments, Dunedin, New Zealand).

Data Analysis

Hemodynamic data were averaged for 10 cycles of non-PLSA or 3 min of PLSA data. The pulsatility index (PI) was analyzed for these cycles by calculating the difference between the maximum and minimum total aortic flow and dividing value by the total aortic flow average. Energy equivalent pressure (EEP) and surplus hemodynamic energy (SHE) as defined by Soucy *et al.*[14] were also calculated to better quantify the dynamic energy of the system. The transvalvular pressure (TVP) is calculated by subtracting the LVP waveform from the AoP waveform; the aortic valve flow (AVQ) is calculated by subtracting the LVAD flow signal from the total aortic flow. Both TVP and AVQ were calculated at each time point, valve opening is analyzed from the hemodynamic tracings using a customized analysis. A MATLAB (Mathworks, Natick, MA) algorithm was developed to analyze AVO using two different hemodynamic signals—TVP and AVQ. Each algorithm analyzed 10 cardiac cycles for non-PLSA conditions and 60 s for those with PLSA conditions. Both

Table 1. Hemodynamics of Non-PLSA Conditions

Conditions	LVP (mm Hg)	AoP (mm Hg)	Total Flow (L/min)	LVADQ (L/min)	AVQ (L/min)	*Q* Ratio	PI	SHE (mm Hg)	EEP (ergs/cm^3)
CS Off									
6k	9.3±0.1	36.3±0.5	2.6±0.1	2.4±0.1	0.1±0.1	1.0	0.0	0.0±0.0	0.0±0.0
7k	9.2±0.1	46.1±0.3	3.0±0.2	2.9±0.0	0.1±0.2	1.0	0.0	0.0±0.0	0.0±0.0
8k	9.0±0.1	57.4±0.2	3.5±0.2	3.4±0.0	0.1±0.2	1.0	0.0	0.0±0.0	0.0±0.0
9k	8.7±0.1	69.8±0.3	4.0±0.2	3.9±0.0	0.0±0.2	1.0	0.0	0.0±0.0	0.0±0.0
10k	8.5±0.1	84.0±0.3	4.4±0.2	4.4±0.0	0.0±0.0	1.0	0.0	0.0±0.0	0.0±0.0
11k	8.2±0.1	100.0±0.4	4.9±0.2	4.9±0.0	0.0±0.0	1.0	0.0	0.0±0.0	0.0±0.0
CS Low									
Off	24.1±23.5	42.7±17.6	2.8±0	0.0±0.0	2.8±5.3	0.0	6.1	5542.3±562.8	45.7±0.5
6k	23.9±23.5	51.6±10.6	3.2±4.3	2.1±2.1	1.1±2.6	0.6	4.1	2918.5±151.4	53.8±0.2
7k	24.7±24.6	58.9±7.8	3.4±3.5	3.0±2.2	0.4±1.0	0.9	3.2	1872.2±299.3	60.4±0.2
8k	24.8±25.1	68.9±4.6	3.8±2.8	3.7±2.3	0.2±0.7	1.0	2.2	1477.5±180.8	70.6±0.2
9k	24.5±24.8	80.6±4.7	4.3±2.2	4.2±2.2	0.1±0.6	1.0	1.9	1269.8±159.2	82.5±0.0
10k	22.8±23.8	94.5±4.7	4.6 2.6	4.6±2.1	0.0±0.6	1.0	1.7	1222.3±88.8	96.3±0.1
11k	22.1±23.2	109.8±4.7	5.1±2.5	5.1±2.0	0.0±0.5	1.0	1.5	974.1±82.5	111.7±0.2
CS Med									
Off	31.0±34.6	60.5±23.0	3.5±6.9	0.0±0.1	3.6±6.9	0.0	6.1	6831.1±612.8	64.9 ± 0.5
6k	30.1±33.7	63.5±17.2	3.8±6.9	1.6±2.6	2.2±4.6	0.4	5.5	8871.2±472.9	70.4±0.4
7k	30.5±34.6	69.9±14.6	4.0±5.9	2.4±2.7	1.7±4.6	0.6	4.5	6685.0±741.0	75.4±0.5
8k	31.4±35.7	77.9±11.8	4.1±5.0	3.2±2.9	0.9±2.5	0.8	3.8	3954.3±413.0	81.4±0.3
9k	32.4±36.9	86.9±8.4	4.4±4.1	4.1±3.0	0.3±1.3	0.9	2.9	2703.6±96.7	89.8±0.1
10k	32.2±37.1	100.2±6.8	4.9±3.7	4.7±3.0	0.2±0.8	1.0	2.2	2294.7±94.6	103.1±0.1
11k	30.8±36.1	115.2±6.9	5.2±3.6	5.2±2.9	0.0±0.8	1.0	2.0	2173.7±113.1	118.5±0.1

AoP, aortic root pressure; AVQ, aortic valve flow; CS, cardiac simulator; EEP, energy equivalent pressure; LVADQ, left ventricular assist device flow; LVP, left ventricular pressure; PI, pulsatility index; PLSA, programmed low speed algorithm; SHE, surplus hemodynamic energy.

algorithms utilized a zero crossing method to determine when the AV opened or closed. Once the algorithm determined these opening and closing points, the absolute opening time for each LVAD speed was calculated (OT-TVP [opening time-transvalvular pressure]). For PLSA conditions, the FSP and LSP opening times were separated into two different arrays to be analyzed separately. Values for each PLSA and non-PLSA condition were then averaged and a standard deviation was calculated. LVAD "backflow" was calculated using the same method, by analyzing the LVAD flow signal for the zero crossing and calculating the duration and magnitude of negative flow.

During the experimental data collection, a Nikon 1 s1 (Nikon corporation, Chiyoda, Tokyo) high-speed camera at a 640×240 pixel area acquired live video recording at 400 frames per second using a. A separate MATLAB (Mathworks, Natick, MA) algorithm was generated to analyze the videos recorded separately. The script analyzed 5 s of the non-PLSA conditions. The raw videos were imported into MATLAB, split into still frames and cropped to only show the AV, which we termed the region of interest (ROI). A Gaussian low-pass filter (3×3, sigma = 0.5) was applied to the ROI to filter out the high frequency noise. The ROI was then converted to grayscale through the elimination of hue and saturation information but still retaining the luminance. A user defined circle was drawn over the valve, and all pixels located outside of the circle were colored black. Otsu's method[15] was employed automatically

Table 2. Results from Aortic Valve Biomechanics Measurement (High Speed Video)

Conditions	OT-AVQ (ms)	OT-TVP (ms)	OT-VID (ms)	Max Area (mm^2)	Percent Area (%)	VO (#/min)
CS Low						
Off	304±5	265±0	321±3	148±1	100	70
6k	250±8	190±4	262±1	131±2	89	70
7k	213±10	143±8	228±2	107±2	72	70
8k	NA	NA	NA	NA	NA	NA
9k	NA	NA	NA	NA	NA	NA
10k	NA	NA	NA	NA	NA	NA
11k	NA	NA	NA	NA	NA	NA
CS Med						
Off	295±4	263±3	304±1	165±2	100	70
6k	278±15	222±3	273±0	160±1	97	70
7k	249±8	199±2	259±2	152±1	92	70
8k	221±4	164±4	230±1	132±2	80	70
9k	185±7	123±6	176±6	66±5	40	70
10k	NA	NA	NA	NA	NA	NA
11k	NA	NA	NA	NA	NA	NA

AVQ, aortic valve flow; CS, cardiac simulator; OT, opening time; TVP, transvalvular pressure; VO, valve opening.

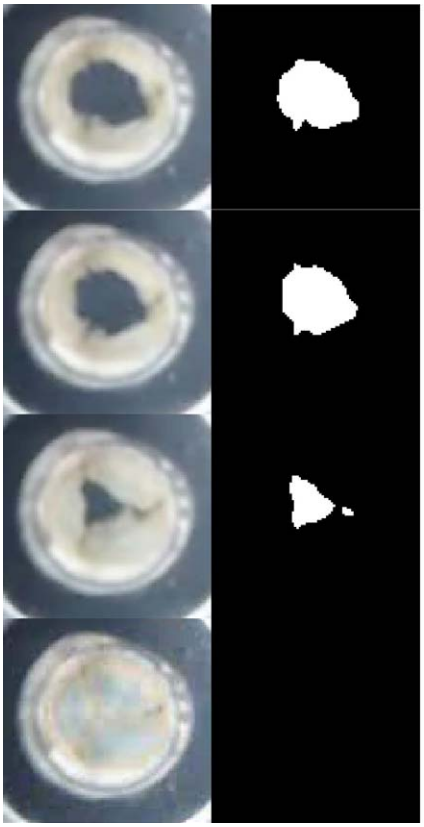

Figure 2. Valve images during the cardiac simulator (CS) Med level of cardiac function illustrate how the maximum valve opening area is decreased gradually with increasing left ventricular assist device (LVAD) support. full color online

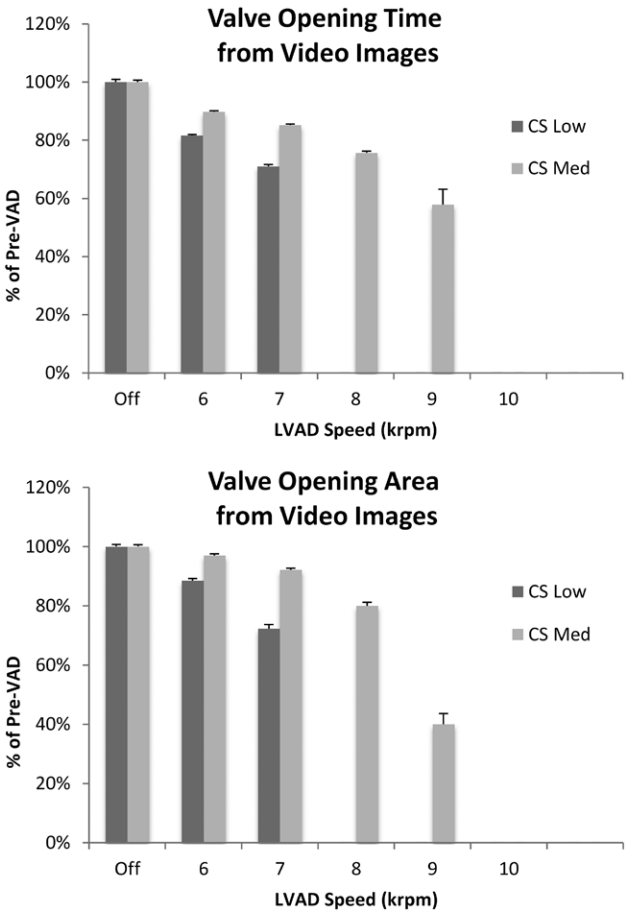

Figure 3. Valve opening time (top) and maximum area (bottom) are shown as a percent change from baseline (pre-left ventricular assist device [pre-LVAD]) conditions. A consistent decrease is seen with increased LVAD speed for all levels of cardiac function for both parameters, but the decline in area is steeper than the opening time.

on each frame, and the effectiveness of this method was determined. If the effectiveness of Otsu's method was more than 70%, the frame would be identified as a frame with AV opening, and the frame would be converted into a binary image using a predefined threshold of 0.13. If Otsu's method was under the 70% effectiveness the AV would be considered closed. The binary conversion resulted in an image with only white pixels for the AV's opening area, all other pixels were black. The white pixels in each frame were automatically counted and converted to millimeter squared as value for the opening area. To determine the actual opening time the frames that showed opening were counted per cardiac cycle. This number of frames was then multiplied by the key frame rate that resulted in an opening time for systole (OT-VID). A peak detections algorithm was employed to determine maximum opening area for each cardiac cycle. All these found values were averaged, and the standard deviation was calculated.

Results

The average hemodynamic indices for all non-PLSA flow conditions are shown in **Table 1**. These results generally agree with our previous studies and establish a baseline for comparison with the PLSA conditions. The pre-LVAD hemodynamics were measured while the LVAD was off and the conduit was clamped, allowing the characterization of NYHA status. In these studies, the CS Low level of cardiac function corresponded to a cardiac output of 2.8 L/min, stroke volume of 40 ml, ejection fraction of 22%, and systolic duration of 35% of the cardiac cycle. The CS Med level produced a cardiac output of 3.5 L/min, corresponding to a stroke volume of 50 ml, ejection fraction of 28%, and systolic duration of 35%. With the addition of the LVAD to the system, aortic

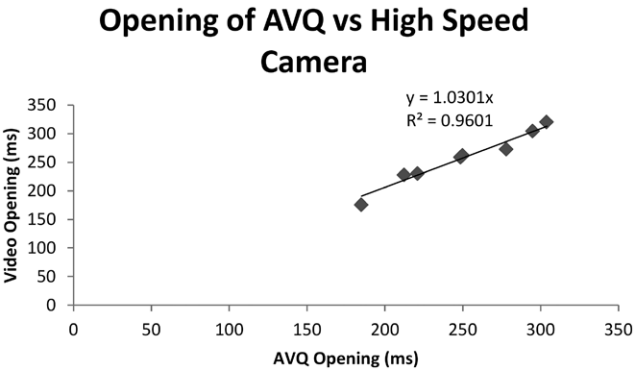

Figure 4. The valve opening time was calculated from the aortic valve flow signal, and these measurements correlated to those obtained from the high-speed video camera. The excellent correlation validates the use of the flow signal to measure valve opening time. AVQ, aortic valve flow.

flow and pressure were augmented as LVAD speed increased, resulting in an increased average TVP. The ratio between LVAD and total aortic flows provides an index of the mode of flow—parallel or series—through the LVAD-heart system.

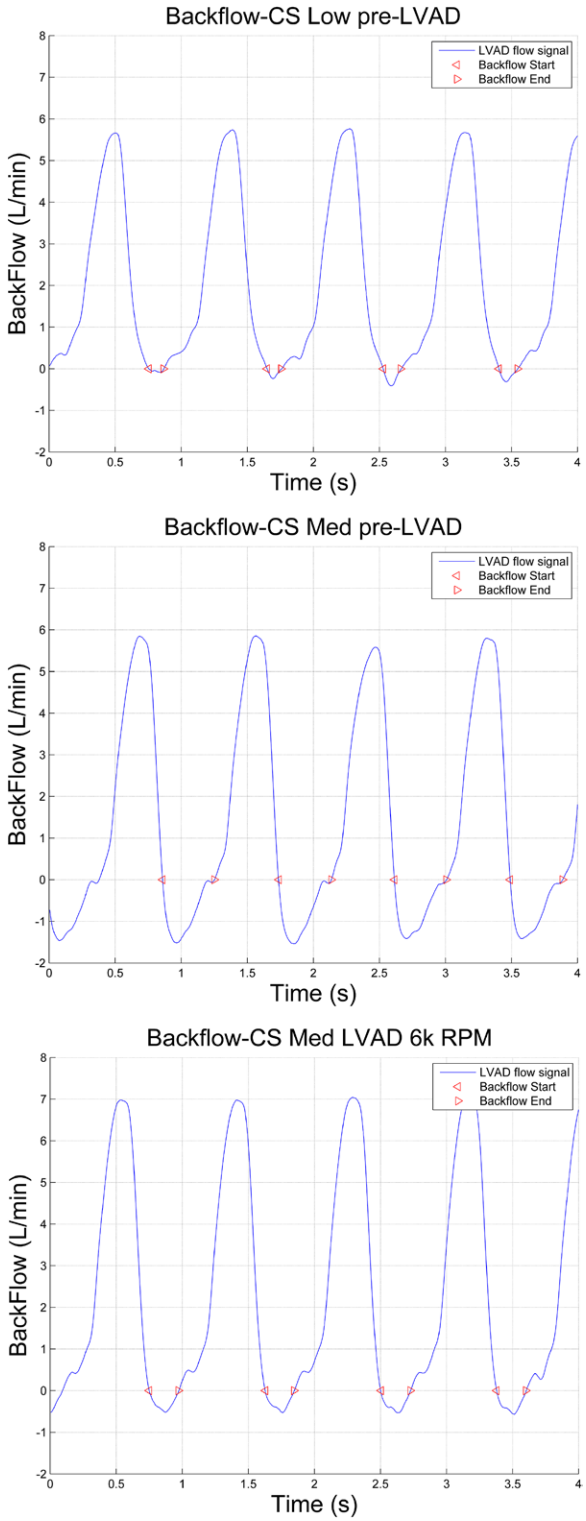

Figure 5. Left ventricular assist device (LVAD) backflow was calculated as the duration and peak of negative LVAD flow and was observed under only three flow conditions as shown in this figure. CS, cardiac simulator; RPM, revolutions per minute.

During the Pre-LVAD condition, there is no LVAD flow hence the *Q* ratio is zero. In the absence of cardiac function (CS Off), the aortic valve is continuously closed, the *Q* ratio is

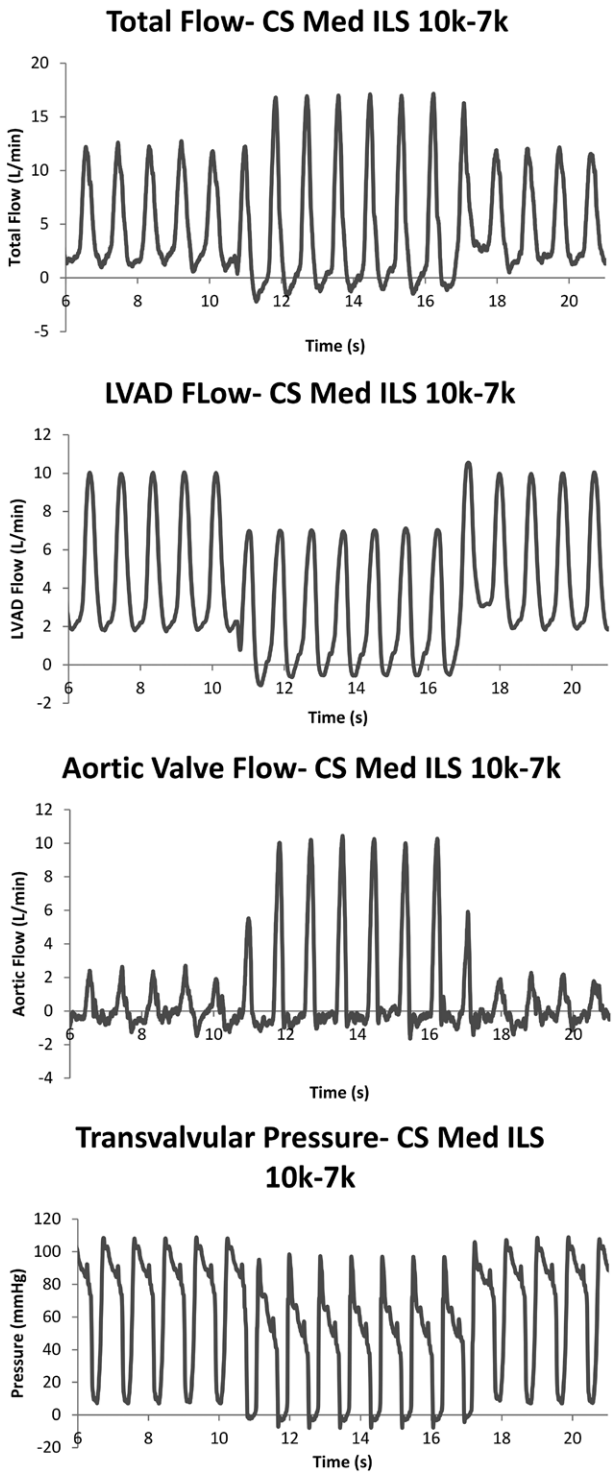

Figure 6. The total flow and left ventricular assist device (LVAD) flow signals measured during the transition from a fixed speed of 10 krpm to a low speed of 7 krpm are shown for the cardiac simulator (CS) Med cardiac condition. The aortic valve flow signal is calculated by subtracting left ventricular assist device (LVAD) from total flow, and transvalvular pressure was calculated by subtracting aortic pressure from left ventricle (LV) pressure.

1.0, evidencing a series flow condition. However, when the flow field is parallel, the *Q* ratio denotes the fraction of the total flow that occurs through the LVAD and, by inference, the flow fraction through the aortic valve. As can be observed from the table, the transition from series to parallel occurs gradually, with complete valve closure for the CS Low condition taking place between 7 and 8 krpm, and between 9 and 10 krpm for CS Med. A threefold decrease in the PI is observed over the range of LVAD support for both series levels of cardiac function. As LVAD speed was increased, EEP more than doubled for CS Low and increased by 75% for CS Med, whereas a significant decrease was witnessed in SHE for both levels of cardiac contractility. **Table 2** provides the measurements of valve biomechanics from both the high-speed video and hemodynamics signals. The maximum opening area (**Figure 2**) and systolic duration for both Pre-LVAD conditions were similar and used to define 100% opening for the remaining conditions at the same level of cardiac function. Image-based results showed that both the valve opening time and opening area (Max Area) decreased with increasing LVAD speeds for parallel conditions, despite the valve opening frequency remaining constant. Once the transition to series flow occurred, no further valve opening was observed. For the CS Low condition, **Figure 3** illustrates that no AVO occurred until the LVAD speed dropped to 7 krpm, at which a valve opening time of 71% and max area of 72% baseline were achieved, allowing 28% of total flow through the aortic valve. The CS Med condition, with the increased level of LV function, produced valve opening at an LVAD speed of 9 krpm, which was 58% baseline opening time but only 40% baseline max opening area, flow through the aortic valve was 10% of the baseline. When the LVAD speed was lowered to 7 krpm, 85% of the baseline opening time and 92% of the max opening area were achieved with 40% of the total flow going through the aortic valve. The hemodynamic method for detecting valve opening time was accurate within 5% of the video based measurements and well correlated as shown in **Figure 4** ($R_2 = 0.96$).

No backflow was observed for CS Low flow conditions until the LVAD speed dropped to 6 krpm, at which negative LVAD flow was observed for 93 ± 11 ms and peaked at −0.25 ± 0.08 L/min. For CS Med conditions, backflow of 218 ± 4 ms duration and 0.48 ± 0.02 L/min was observed at a speed of 7 krpm, and 361 ± 21 ms and 1.43 ± 0.09 L/min at 6 krpm. These results are shown in **Figure 5**.

The effect of the PLSA control on pulsatility of pressure and flow is illustrated for a single flow condition (10k_7k) in **Figure 6** and summarized for all PLSA conditions in **Table 3**. **Table 3** illustrates that the PI increases when the LVAD speed is decreased from FSP to LSP indicating the ability of the PLSA algorithm to decrease flow stasis, particularly in the aortic root. **Figure 6** shows that during a decrease in LVAD speed from 10

Table 3. Hemodynamics of PLSA Conditions

Conditions	LVP (mm Hg)	AoP (mm Hg)	Total Flow (L/min)	LVADQ (L/min)	AVQ (L/min)	*Q* Ratio	PI FSP	PI LSP
CS Off								
8k_6k	9.0±0.2	54.7±7.6	3.4±0.5	3.3±0.4	0.0±0.2	1.0	0.0	0.0
9k_6k	8.8±0.3	65.3±11.1	3.8±0.7	3.7±0.7	0±0.2	1.0	0.0	0.0
10k_6k	9.6±0.5	77.8±15.6	4.2±0.9	4.2±0.9	0±0.2	1.0	0.0	0.0
11k_6k	8.4±0.5	89.8±22.2	4.5±1.1	4.5±1.1	0.0±0.2	1.0	0.0	0.0
9k_7k	8.8±0.2	66.6±7.9	3.8±3.8	3.8±0.5	0.0±0.2	1.0	0.0	0.0
10k_7k	8.6±0.3	78.8±12.7	4.2±0.7	4.2±0.7	0.0±0.2	1.0	0.0	0.0
11k_7k	8.4±0.5	92.3±18	4.6±1.0	4.6±0.9	0.0±0.2	1.0	0.0	0.0
9k_8k	8.8±0.1	68.1±4.1	3.9±0.3	3.9±0.2	0.0±0.2	1.0	0.0	0.0
10k_8k	8.6±0.2	80.5±8.8	4.3±0.5	4.3±0.5	0.0±0.2	1.0	0.0	0.0
11k_8k	8.3±0.3	94.1±14.0	4.7±0.8	4.7±0.7	0.0±0.2	1.0	0.0	0.0
CS Low								
8k_6k	24.9±25.2	66.8±7.7	3.8±3.1	3.5±2.3	0.3±1.1	0.9	2.1	4.7
9k_6k	24.1±24.6	77±10.7	4.1±3.0	3.9±2.3	0.2±1.1	1.0	1.9	4.4
10k_6k	23.1±23.9	90±13.6	4.5±2.9	4.4±2.3	0.3±1.0	1.0	1.7	4.3
11k_6k	22.1±23.4	102.5±18.9	4.9±2.8	4.8±2.3	0.1±1.0	1.0	1.4	3.7
9k_7k	24.1±24.7	77.8±8.6	4.1±2.9	4±2.3	0.1±0.8	1.0	1.9	3.3
10k_7k	23.2±24.1	89.5±12.7	4.5±2.8	4.4±2.2	0.1±0.8	1.0	1.7	3.2
11k_7k	22.3±23.6	102.7±17.4	4.9±2.7	4.8±2.2	0.1±0.7	1.0	1.4	3.1
9k_8k	24±24.7	79±6.1	4.2±2.8	4.1±2.2	0.1±0.6	1.0	1.9	2.2
10k_8k	23.1±24.1	91±9.6	4.6±2.6	4.5±2.2	0.0±0.6	1.0	1.6	2.4
11k_8k	22.1±23.4	104.2±14.2	5±2.6	4.9±2.1	0.0±0.5	1.0	1.4	2.1
CS Med								
8k_6k	31.3±35.6	76.3±13.3	4.0±5.3	3.0±2.9	1.0±2.9	0.8	3.9	5.6
9k_6k	32.3±36.7	84.2±12.2	4.3±4.5	3.8±3.1	0.5±2.1	0.9	2.9	6.3
10k_6k	31.9±30.7	95.9±14.2	4.7±4.2	4.3±3.1	0.4±1.9	0.9	2.3	5.7
11k_6k	31.0±36.0	107.5±19.8	5.0±4.3	4.7±3.2	0.4±2.0	0.9	2.0	5.5
9k_7k	32.2±36.8	85.0±10.8	4.3±4.4	3.9±3.0	0.4±1.8	0.9	2.9	5.2
10k_7k	32.0±36.9	96.8±12.2	4.7±4.1	4.5±3.1	0.5±1.5	0.9	2.3	4.6
11k_7k	31.0±36.2	109.4±17.0	5.1±4.0	4.8±3.1	0.3±1.6	0.9	2.0	4.8
9k_8k	32.4±37.0	86.0±9.4	4.4±4.2	4.0±3.0	0.4±1.6	0.9	2.9	4.1
10k_8k	32.1±37.0	97.4±10.5	4.7±3.9	4.5±3.0	0.2±1.2	1.0	2.2	4.1
11k_8k	31.0±36.3	110.7±14.3	5.1±4.8	5.0±3.0	0.1±1.1	1.0	2.0	4.0

AoP, aortic root pressure; AVQ, aortic valve flow; CS, cardiac simulator; FSP,fixed speed; LSP, low speed; LVADQ, left ventricular assist device flow; LVP, left ventricular pressure; PI, pulsatility index for fixed speed and low speed PLSA, programmed low speed algorithm.

to 7 krpm during PLSA control, PI in the distal aorta is approximately doubled. In addition, high pulsatility flow through the aortic valve is produced during the DwT, but with a minimal (<5%) reduction in cardiac output. The TVP signal dropping below zero corresponds to the increase from zero in flow through the aortic valve (AVQ) during AVO.

For CS Low, AVO is produced when the LVAD speed drops below the threshold between series and parallel flow, which is seen for all seven conditions when the low speed is 7 krpm or less. Compared with a constant LVAD speed of 10 krpm, the valve opening during 10k_7k increased from nothing to 7 times/min, whereas total aortic flow remains essentially unchanged. The 10k_8k condition did not produce parallel flow in combination with the CS Low level of cardiac function. The CS Med condition produced a transition from series to parallel flow between 10 and 9 krpm. Compared with a constant LVAD speed of 10 krpm, both 10k_8k and 10k_7k PLSA conditions produced parallel flow during the dwell period, enabling AVO, which was greater with the lower dwell speed. These conditions showed an increase in pulsatility with a minimal decrease of total aortic flow and minimal backflow through the LVAD.

Figure 7 and **Table 3** show how flow through the aortic valve is modulated during the PLSA conditions with the CS Med level of cardiac function, demonstrating that when the low speed is below 9 krpm, several large pulsatile cycles of flow are enabled to wash the aortic outflow tract and root, without affecting overall cardiac output. Even when the flow is parallel throughout the entire PLSA sequence, greater pulsatility is achieved during the dwell speed time.

Discussion

A new control algorithm for the HM II LVAD was tested on a mock circulatory loop at SDSU. The results show that the PLSA enables intermittent AVO and flow through the valve orifice, as well as increasing pulsatility in the aortic root, during conditions in which the valve would otherwise be continuously closed. Changes in PI, EEP, and SHE were measured reflecting a significant reduction in the pulsatile nature of the flow. These trends compare favorably with changes in pulsatility measured in human continuous flow LVAD patients by Travis *et al*.[13] By reducing the LVAD speed to the LSP setting, an intermittent increase in vascular pulsatility is introduced for several cycles each minute. Restoring pulsatility on a periodically rhythmic basis addresses two potential problems with LVAD support: 1) lack of valve opening, which has been associated with AI, and 2) poor blood mixing in the aortic root, which has been associated with thromboembolic events in these patients.[16,17]

The control of CF-LVADs has historically ranged from simple fixed speeds (the currently approved operating mode in the HM II) to emulation of complex physiologic responses. The first successful feature developed to augment fixed LVAD speed was suction control.[18] Since that time, increasing complexity such as adding pulsatility, a Frank–Starling response, and feedback control with sensors, such as pressure and flow, have been attempted but not gained widespread acceptance.[19–24] Some effort has been made to modulate aortic valve flow and opening in the Jarvik CF-LVAD by reducing LVAD speed periodically. Using an animal model, Tuzun *et al*.[25] assessed the effects of the Jarvik 2000 on AVO and pump outflow when operated in intermittent low speed (ILS) mode. They demonstrated that AVO and ejection could be successfully achieved by temporarily reducing the pump speed for 10 s each minute (*i.e*., operating the pump in ILS mode), even in states of low cardiac output associated with total closure of the aortic valve. This allowed the aortic valve to open 6 times/ min during a 60 bpm cardiac cycle.

The results of this study show that the LVAD speed at which the aortic valve opens varies depending on the level of native cardiac contraction, but that valve opening was observed at a speed of 7 krpm for all pulsatile conditions tested. However, valve opening frequency is an inadequate measure of valve opening, as the valve opening (systolic) duration and maximum orifice area also decrease with LVAD speed, which directly affects the flow through the aortic valve during LVAD support.

Limitations

The mock loop in this study has a fixed resistance and does not include closed-loop feedback that mimics autoregulation

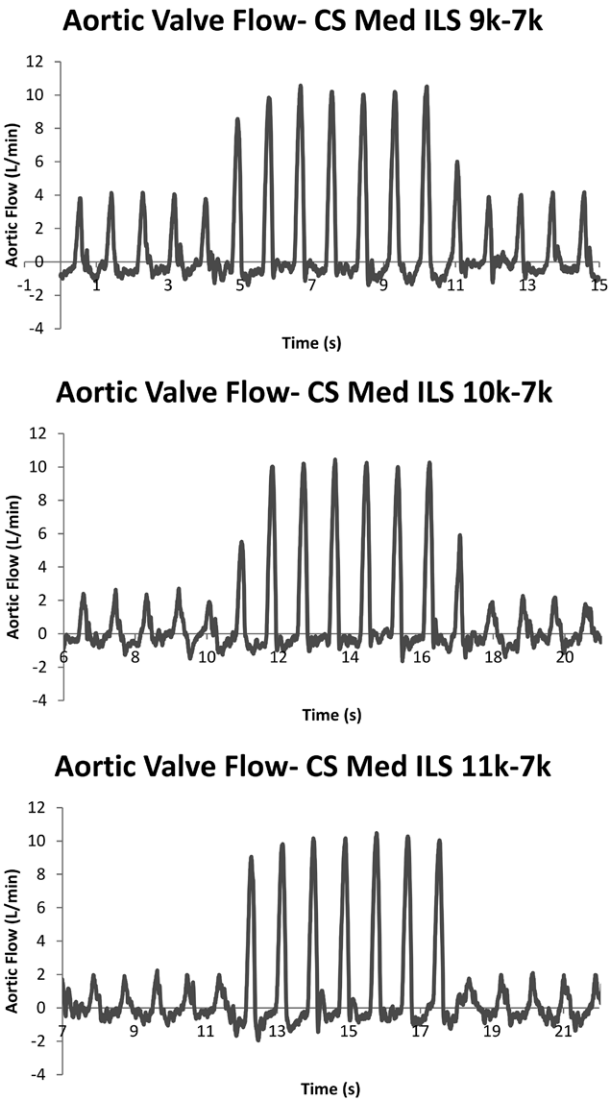

Figure 7. Flow through the aortic valve calculated for several different fixed speed conditions is shown, illustrating the high pulsatility of the flow during the low speed period, even when flow through the valve occurs at the fixed speed (9k_7k).

of blood pressure or the Frank–Starling effect. Thus, additional studies are needed to verify these adaptive responses not only in a mock circulation, but also in animals where these feedback mechanisms are completely intact. The reproducibility of the system is useful in characterizing the mechanical response to PLSA over a large matrix of experimental conditions in a well-controlled subject. Once the optimal range of settings is identified, these further studies can be better targeted to achieving the best clinical practice.

Conclusion

The PLSA control algorithm is designed to produce intermittent valve opening in the LVAD supported heart, without substantially decreasing the cardiac output. The studies performed in the mock loop show that programmed speed reduction to 7 krpm was successful in producing AVO under all pulsatile conditions, with a minimal change (<5%) in cardiac output. Furthermore, aortic flow pulsatility quadrupled in the aortic root and doubled in the distal aorta during PLSA conditions, providing evidence that AVO and blood mixing are enabled by PLSA control at the appropriate speed.

Acknowledgment

The authors appreciate the assistance of Vi Vu in conducting the studies and analyzing the results. Supported by the Thoratec Corporation.

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