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Preservation Of Native Aortic Valve Flow And Full Hemodynamic Support With The TORVAD™ Using A Computational Model Of The Cardiovascular System

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Abstract

This paper describes the stroke volume selection and operational design for the TORVAD™, a synchronous, positive-displacement ventricular assist device (VAD). A lumped parameter model was used to simulate hemodynamics with the TORVAD™ compared to those under continuous flow VAD support. Results from the simulation demonstrated that a TORVAD™ with a 30 mL stroke volume ejecting with an early diastolic counterpulse provides comparable systemic support to the HeartMate II® (HMII) (cardiac output 5.7 L/min up from 3.1 L/min in simulated heart failure). By taking advantage of synchronous pulsatility, the TORVAD™ delivers full hemodynamic support with nearly half the VAD flow rate (2.7 L/min compared to 5.3 L/min for the HMII) by allowing the left ventricle to eject during systole, thus preserving native aortic valve flow (3.0 L/min compared to 0.4 L/min for the HMII, down from 3.1 L/min at baseline). The TORVAD™ also preserves pulse pressure (26.7 mmHg compared to 12.8 mmHg for the HMII, down from 29.1 mmHg at baseline). Preservation of aortic valve flow with synchronous pulsatile support could reduce the high incidence of aortic insufficiency and valve cusp fusion reported in patients supported with continuous flow VADs.

Introduction

Ventricular assist devices (VADs) are increasingly used in the treatment of end-stage heart failure. They are implanted often as a bridge-to-transplant and, more recently, as destination therapy, as well as bridge-to-recovery.[1] Continuous flow (CF) VADs, like the HeartMate II® (Thoratec Corporation, Pleasanton, CA) and the HVAD® (HeartWare Inc, Framingham, MA), have come to dominate clinical applications, increasing from 72% of VAD implants in 2008 to 100% in 2013 according to the Interagency Registry for Mechanically Assisted

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Circulatory Support (INTERMACS) database.[1] Continuous flow VADs are most commonly operated in a fixed revolutions per minute (rpm) mode wherein blood is continuously pumped from the left ventricle to the aorta at a flow rate dependent on the differential pressure across the pump. As the differential pressure decreases, the flow rate increases, and vice versa. As a result of this relationship, the flow is highest through the device during systole when the left ventricle is contracting and much of the blood flow that would normally be ejected and go through the aortic valve is instead shunted through the CF VAD. As native aortic flow is "stolen" by the CF VAD, the aortic valve will often cease to open. While CF VAD patient outcomes have improved as clinicians have become more familiar and experienced with the technology, problems remain. Elevated device shear rates in CF VADs have been associated with acquired von Willebrand syndrome (with serious bleeding complications in 40% of VAD patients)[2], platelet activation associated thrombus formation[3], and white blood cell alterations that may increase a patient's vulnerability to infection.[4,5] Driveline infection rates are common as transcutaneous energy transfer challenges remain due in part to the internal battery requirements necessary for CF VAD power consumption[6]. Aortic valve commissural fusion and aortic insufficiency (AI) are frequently observed in CF VAD recipients, especially in patients whose aortic valves fail to open for prolonged periods of time.[7–10] Single-center incidence rates for development of AI has been reported[11–14] to range between 14.3% and 51%, and commissural fusion rates exceed 50% in some reports.[15–17] The pathogenesis of valve commissural fusion has been attributed to altered biomechanics when the aortic valve fails to open or opens infrequently in CF VAD recipients.[18] Insufficient or infrequent opening of the aortic valve can also lead to aortic root and left ventricular outflow tract thrombosis.[19,20] A pump with lower shear, lower power requirements, and one that allows frequent aortic valve opening could alleviate these problems.

The TORVAD™ (Windmill Cardiovascular Systems Inc., Austin, TX) is a valveless positive-displacement VAD that can deliver precisely timed ejections synchronized to the cardiac cycle using two independently controlled pistons traveling within a torodial pumping chamber. Rotational speeds are low, approximately 90 rpm, and vary with the native heart rate, which should result in low shear compared to CF VADs operating at several thousand rpm. A schematic of the pump along with a graphical depiction of its cardiac synchronization can be seen in Figure 1 and Figure 2. Synchronization is utilized to control critical hemodynamics such as cardiac output, aortic valve flow, and pulse pressure.[21] If needed, the TORVAD™ can automatically pump asynchronously to deliver up to 8 L/min in the case of cardiac electrical instability. The first generation of the device, tested in acute animal porcine experiments, had a stroke volume of 37.5 mL.[22] The goal of this paper is to describe how an appropriate pump stroke volume and timing of synchronous pumping was determined for optimal circulatory support in the majority of patients in need of a VAD. This design approach made use of a computational model of the cardiovascular system.

Computational modeling, from complex three-dimensional fluid-structure interaction simulations to simplified lumped-parameter models, are extensively used in VAD design to save both the cost and time of fabricating and testing multiple iterations of devices. Lumped-parameter models of the cardiovascular system represent spatially distributed physical

effects using discrete elements to approximate the behavior of the system. This approach is commonly adopted to assess cardiovascular hemodynamics with a VAD.[23–30]

Methods

A lumped-parameter model[31] of the cardiovascular system was used in this study. The model was a closed cardiovascular system loop and included elements that allowed assessment of the pressure and flow in the systemic and pulmonary arterial and venous systems as well as in the ventricles and atria. The model was previously verified for comparing the hemodynamic effects of a CF VAD to the TORVAD™ using *in vivo* data. The details of this model have been previously reported,[31] so only a brief overview of the critical elements in the model is provided herein.

Cardiovascular System Model

The pressure in the heart chambers was modeled using passive[32] and active[33,34] elastance functions and unidirectional flow was enforced by using fluidic diode models with nonlinear resistance.[35] The systemic and pulmonary systems were modeled on the basis of the unsteady Bernoulli equation incorporating vessel resistance, compliance, and blood inertia,

$$P = \frac{Q_{\text{in}} - Q_{\text{out}}}{C}$$

$$Q = \frac{\Delta P - RQ}{L}$$

where P is the pressure in the vessel, Q_{in} is the flow into the vessel, Q_{out} is the flow out of the vessel, C is the compliance, R is the resistance, and L is the fluid inertia. Model parameters used to simulate moderate congestive heart failure (HF) can also be found in the previously referenced article.[31] The heart rate in HF is elevated and often remains elevated after a VAD is implanted[36], therefore 90 beats per minute was used in this model. While linear models are assumed here, this is not a necessary requirement as the model was simulated by computational means.

Ventricular Assist Device Models

As previously mentioned, the TORVAD™ is a positive-displacement pump that delivers synchronous ejections of a known stroke volume at a predetermined time during the cardiac cycle. The pump does not have a compliance chamber, but instead it aspirates blood from the left ventricle and ejects blood into the aorta simultaneously and at the same flow rate. Synchronous pumping is accomplished using epicardial pacemaker leads to sense ventricular depolarization, which then triggers the pumping cycle. The leads are placed directly on the right ventricular myocardium, which avoids cardiac conduction abnormalities such as a wide complex or left bundle branch block that would affect a surface electrocardiogram (ECG) and cause triggering problems for other synchronous support

technologies (like an intra-aortic balloon pump). The TORVAD™ can be controlled to follow any flow rate profile; for this study the flow rate followed a sinusoidal curve,

$$Q_{\mathrm{VAD}}=\begin{cases}\frac{2SV}{T_{\mathrm{ST}}}\left(\frac{1}{2}+\frac{1}{2}\cos\left(\frac{2\pi(t-PD\cdot RR)}{T_{\mathrm{ST}}}\right)\right) & \text{if} PD\cdot RR-\frac{T_{\mathrm{ST}}}{2}\le t<PD\cdot RR+\frac{T_{\mathrm{ST}}}{2}\\ 0 & \text{otherwise}\end{cases}$$

where *SV* is the stroke volume, *t* is time normalized to the cardiac cycle with value zero at the R-wave, T_{ST} is the ejection time for a single stroke (300 ms in this study), *RR* is the time interval between successive R-waves and is inversely proportional to the heart rate, and *PD* is the programmable phase delay from the R-wave to the peak ejection flow rate where 0% corresponds to the R-wave, 50% to the mid-point between the current R-wave and the next, and 100% to the next R-wave. Figure 1 provides a graphical depiction of synchronous operation of the TORVAD™ within the cardiac cycle. To determine the stroke volume and synchronous phase needed to support the cardiovascular system in heart failure, stroke volumes between 20 and 50 mL and synchronous phase delays from 0 to 100% were simulated.

The flow rate through the CF VAD is not constant and is modeled by

$$Q_{VAD}=\frac{P_H(\omega,Q_{\mathrm{VAD}})-(P_{\mathrm{ao}}-P_{\mathrm{iv}})-R_{\mathrm{C}}Q_{\mathrm{VAD}}}{L_{\mathrm{C}}}$$

being dependent on the differential pressure across the pump (aortic pressure, P_{ao}, minus left ventricular pressure, P_{lv}) as well as cannula resistance, R_{c}, and the fluid inertia in the cannulas, L_{c}. Cannula resistance and inertia values have been previously described.[31] The functional relationship between pressure, pump speed, and flow, P_H (ω,Q_{VAD}), is described using HeartMate II® (HMII) pressure-flow pump characterization curves at a constant rotational speed. Figure 3 shows the typical clinical range for the HMII and the pressure-flow curve at 9,000 rpm. 9,000 rpm was chosen as the default operation speed for this comparative study because it has been used as the default setting in the controller for the device.[37]

The model equations were implemented in and solved using the commercial software program Matlab® (The MathWorks, Inc., Natick, MA). Critical hemodynamic metrics such as mean cardiac output (CO), mean VAD flow (Q_{VAD}), mean aortic valve flow (Q_{AO}), mean arterial blood pressure (MAP), pulse pressure (PP), left ventricular end-diastolic volume (LVEDV), and mean left atrial pressure (LAP) were time averaged to make comparisons between the different kinds of VAD support.

Results

The cardiovascular model simulation was run in a typical heart failure hemodynamic state. The CO was 3.1 L/min, MAP was 73.7 mmHg, PP was 29.1 mmHg, LVEDV was 244 mL, and LAP was 18.1 mmHg. These values are consistent with VAD eligible heart failure patients.[36,38]

With the HMII simulated at 9,000 rpm, the resultant CO was 5.7 L/min (Q_{VAD} = 5.3 L/min, Q_{AO} = 0.4 L/min), MAP was 78.5 mmHg, PP was 12.8 mmHg, LVEDV was 232 ml, and LAP was 14.1 mmHg. These values are consistent with those of HMII recipients reported in the literature.[39,40]

Next, the TORVAD™ was simulated to run from 0 to 100% phase (during the R-R interval) with stroke volumes ranging from 20 to 50 mL. As mentioned previously, the goal of this study was to determine the optimal phase delay and stroke volume needed to support the circulation at a level comparable to the HMII. A plot of CO versus phase delay at stroke volumes from 20 to 50 mL can be seen in Figure 4. A synchronous phase delay (PD) from 55 to 70% with a stroke volume of 30 mL provided comparable levels of hemodynamic support to the HMII. At 30 mL with a 60% phase delay, the CO was 5.7 L/min (Q_{VAD} = 2.7 L/min, Q_{AO} = 3.0 L/min), MAP was 77.7 mmHg, PP was 26.7 mmHg, LVEDV was 234 mL, and LAP was 14.3 mmHg.

Next, the simulated hemodynamics of the HMII were compared to those induced by the TORVAD™ with a 30 mL stroke volume and a phase delay of 60%. Systemic pressure and flow traces can be seen in Figure 5, and the time-averaged hemodynamics reported above are listed in Table 1 as well as displayed in bar plots in Figure 6. The top row of the bar graphs shows similarities between the pumps regarding levels of circulatory support. Cardiac output, MAP, left ventricular unloading assessed by LVEDV, and LAP were all similarly altered by the introduction of either VAD. The bottom row of the bar graphs shows the ways in which hemodynamic support is different between the two types of pumps. Most notably, the TORVAD™ provides full hemodynamic support with nearly half the VAD flow rate of the HMII (Q_{VAD} = 2.7 L/min for the TORVAD™ and 5.3 L/min for the HMII). This is made possible by the fact that the majority of native aortic valve flow is maintained when using the TORVAD™ as compared to the HMII (Q_{AO} = 3.0 L/min for the TORVAD™ and 0.4 L/min for the HMII, noting that the baseline heart failure cardiac output was 3.1 L/min). This preservation of native aortic flow during TORVAD™ support in contrast to its near elimination during HMII support can be clearly seen on the aortic flow traces in Figure 5.

Discussion

The TORVAD™ is able to provide full hemodynamic support to a simulated cardiovascular system in heart failure with a single 30 mL early diastolic counterpulse compared to the HMII operating at 9,000 rpm. Full support is possible despite the lower VAD flow (2.7 L/min for the TORVAD™ vs 5.3 L/min for the HMII) because the TORVAD™ ceases pumping during systole and allows the ventricle to eject through the aortic valve. In contrast, a CF VAD like the HMII often steals most if not all of the flow that would go through the aortic valve during systole, pumping it instead through the device during ventricular contraction. This effect is illustrated in Figure 2. Native aortic valve flow is preserved with the TORVAD™, which could reduce the incidence of aortic insufficiency, aortic valve cusp fusion, as well as aortic root and left ventricular outflow tract thrombosis, all of which are known complications of CF VAD support.

Native flow through the aortic valve is preserved with TORVAD™, decreasing only slightly from 3.1 to 3.0 L/min despite the reduction in LV volume (234 ml down from 244 ml in baseline heart failure). This relatively small change in aortic valve flow from ventricular contraction is due to the shallow slope of the LV end systolic contraction curve (E_{lv} = 0.30 mmHg/ml), which is much lower than with a healthy ventricle (E_{lv} = 3.25 mmHg/ml), and consequently is less responsive to changes in ventricular volume as compared to a healthy heart. Therefore, the reduction in LVEDV with TORVAD™ support (10 ml) would only result in a 3 mmHg reduction in maximum contractile pressure of the LV, not enough to significantly reduce the native aortic valve flow from LV contraction.

In patients with CF VADs, the so-called Frank-Starling response of CO to changes in preload and afterload, is significantly altered.[41,42] This is likely due to most if not all of the CO being directed through the VAD instead of being controlled by native ventricular contractile ejection through the aortic valve. A VAD that preserves aortic flow, which in turn is at least partially controlled by the Frank-Starling law of the heart, may maintain this important feedback mechanism which would likely have significant implications for patient management and warrants further study. This may be especially important for over pumping and left ventricular wall suction events that can be induced by VADs. The TORVAD™ aspirates from the left ventricle in early diastole when left ventricular volume is lowest, increasing the risk of ventricular suction. Preservation of aortic valve flow and the native Frank-Starling response may minimize the risk of over pumping the ventricle and decrease the risk of ventricular suction.

It is clear that not all patients will fit this model for average heart failure. In clinical practice, patients with varying degrees of heart failure and heart rates receive VADs. The TORVAD™ is adaptable and automatically synchronizes to changes in heart rate. Synchronous support can be maintained for heart rates in excess of 200 bpm if needed, or the pump can be programmed to eject every other heart beat or to transition into asynchronous support if the heart rate exceeds a predetermined value to avoid over pumping that could occur with exercise or ventricular tachycardia. In synchronous operation, the heart rate directly affects the flow rate of the device, so reduced heart rates would lead to reduced mean pump flow rates, which can be cause for concern for thrombus formation in CF VADs. However, the TORVAD™ achieves full pump washout and the same peak flow rate through the device with each stroke, irrespective of heart rate, so a low mean pump flow rate should not increase the risk of thrombus. The TORVAD™ can be programmed to recognize and adapt to arrhythmias, but if synchronous counterpulse support is inadequate for a given patient, the pump can be operated asynchronously up to 8 L/min to provide full circulatory support. When the pump operates at a fixed asynchronous speed, it is likely that the periodicity of the ejections would allow intermittent aortic valve opening, depending on the level of heart failure. On the other hand, if the patient is less sick or if the clinician wishes to exercise the heart as a trial for a potential bridge-to-recovery patient, phasing the ejection later into diastole or into systole or skipping beats may allow for the native ventricle to gradually assume more of the workload in maintaining adequate circulation. These scenarios also warrant additional study.

The TORVAD™ is much smaller than previous sac- or pusher plate-type pulsatile ventricular assist devices and has approximately the same displacement volume as the HMII, which should allow pre-peritoneal placement of the device. In addition, the reduced VAD flow rate requirements of the TORVAD™ as well as the high hydraulic efficiency of a positive displacement pump should enable low power requirements that could make a transcutaneous energy transfer system (TETS) a viable option and lead to longer battery life.

The potential advantages of the TORVAD™ are balanced with potential risks including multiple moving components (two motors and two pistons) as compared to most CF VADs that have a single spinning impeller as well as the necessity of an additional sensor (epicardial ECG lead) for regulating synchronous operation. On the other hand, reduced rotational speeds (mean 90 rpm in synchronous operation) may result in lower shear-based blood trauma such as high molecular weight von Willebrand factor depletion and platelet activation as compared to CF VADs with rotational speeds of thousands or tens of thousands of rpm; *in vitro* hematology experiments will need to be performed to quantify the blood destruction potential. Chronic animal experiments and full system durability will also need to be conducted to assess the safety and reliability of the device.

Conclusion

A computational model of the cardiovascular system has been used to select the stroke volume and synchronous operation mode for the TORVAD™, a synchronous valveless pulsatile ventricular assist device. Using a computational model, a stroke volume of 30 mL with an early diastolic counterpulse ejection was defined as the primary operating mode because it provides similar systemic and ventricular support in terms of CO, MAP, LVEDP, and LAP compared to a CF VAD, while preserving native aortic flow and pulsatility.

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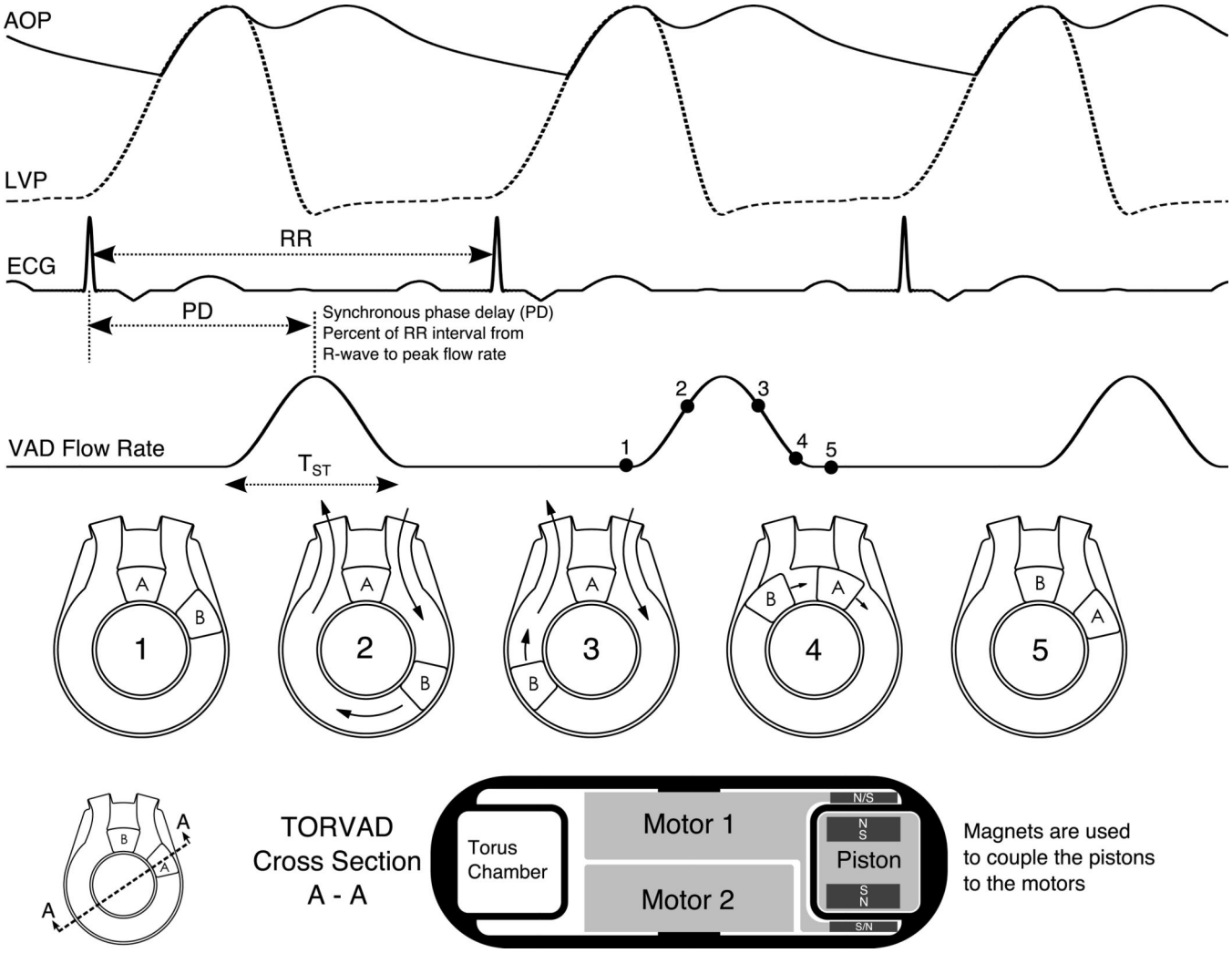

Figure 1.

Hemodynamic plots of aortic pressure (AOP) and left ventricular pressure (LVP), a simulated representation of a typical electrocardiogram (ECG), and a plot of the TORVAD™ flow rate (VAD Flow Rate) are used to demonstrate the synchronous phasing operation of the pump. The R-wave of the ECG and a programmable phase delay (PD) are used to synchronize the peak flow rate of the pump to a predetermined time in the cardiac cycle, in this case early diastole. The effect of this early diastolic ejection (with stroke time T_{ST}) on the arterial pressure can be seen in the AOP trace. This figure also has a schematic representation of the TORVAD™ with two independently controlled pistons, A and B, within a torodial chamber. Pumping is achieved by driving one piston around the chamber while holding the position of the other piston between the inlet and outlet ports to serve as a "virtual" valve. From rest (1), the drive piston (B) begins to rotate (2) based on the programmable phase delay (PD), while the valve piston (A) facilities unidirectional flow. Piston (B) begins to decelerate (3) as it nears completion of a stroke, at which time both pistons move together (4) and then come to rest (5). At this point, the roles of the pistons have been reversed; on the next stroke (A) will act as the drive piston and (B) as the valve

piston. Each piston is comprised of rare earth magnets hermetically-sealed within a titanium jacket and is independently actuated by a position-controlled motor that rotates a C shaped magnetic coupling around the outer surface of the pumping chamber which then drives the respective piston within the torus, as shown in the cross section of the pump.

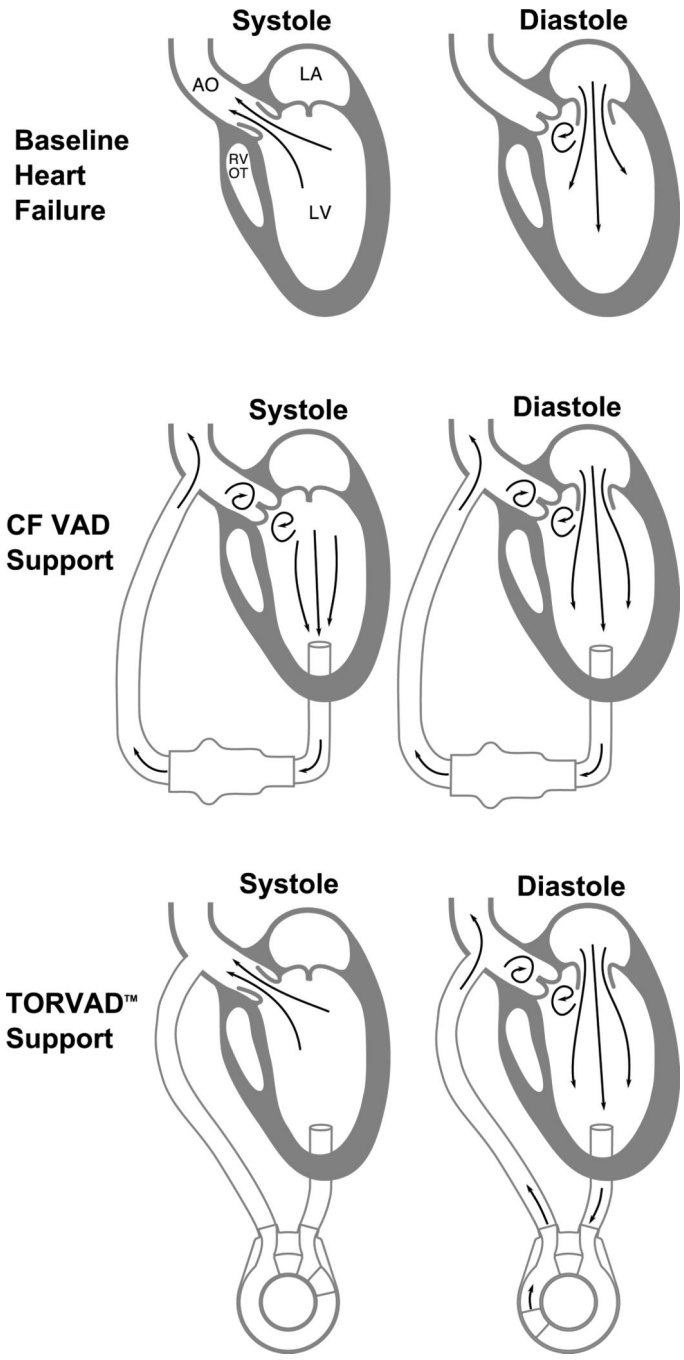

Figure 2.

Depictions of flow in systole and diastole for baseline heart failure, continuous flow (CF) VAD support, and TORVAD™ synchronous counterpulse support. In baseline heart failure without a VAD, blood is ejected from the left ventricle (LV) to the aorta (AO) through the aortic valve in systole. Then the LV is filled from the left atrium (LA) through the mitral valve in diastole. With CF VAD support, the aortic valve will often cease to open in systole because blood flow is shunted through the VAD, leading to continuously recirculating and stagnant flow in the left ventricular outflow tract and aortic root. Native aortic valve flow is

preserved with TORVAD™ synchronous counterpulse support because the pump does not eject in systole.

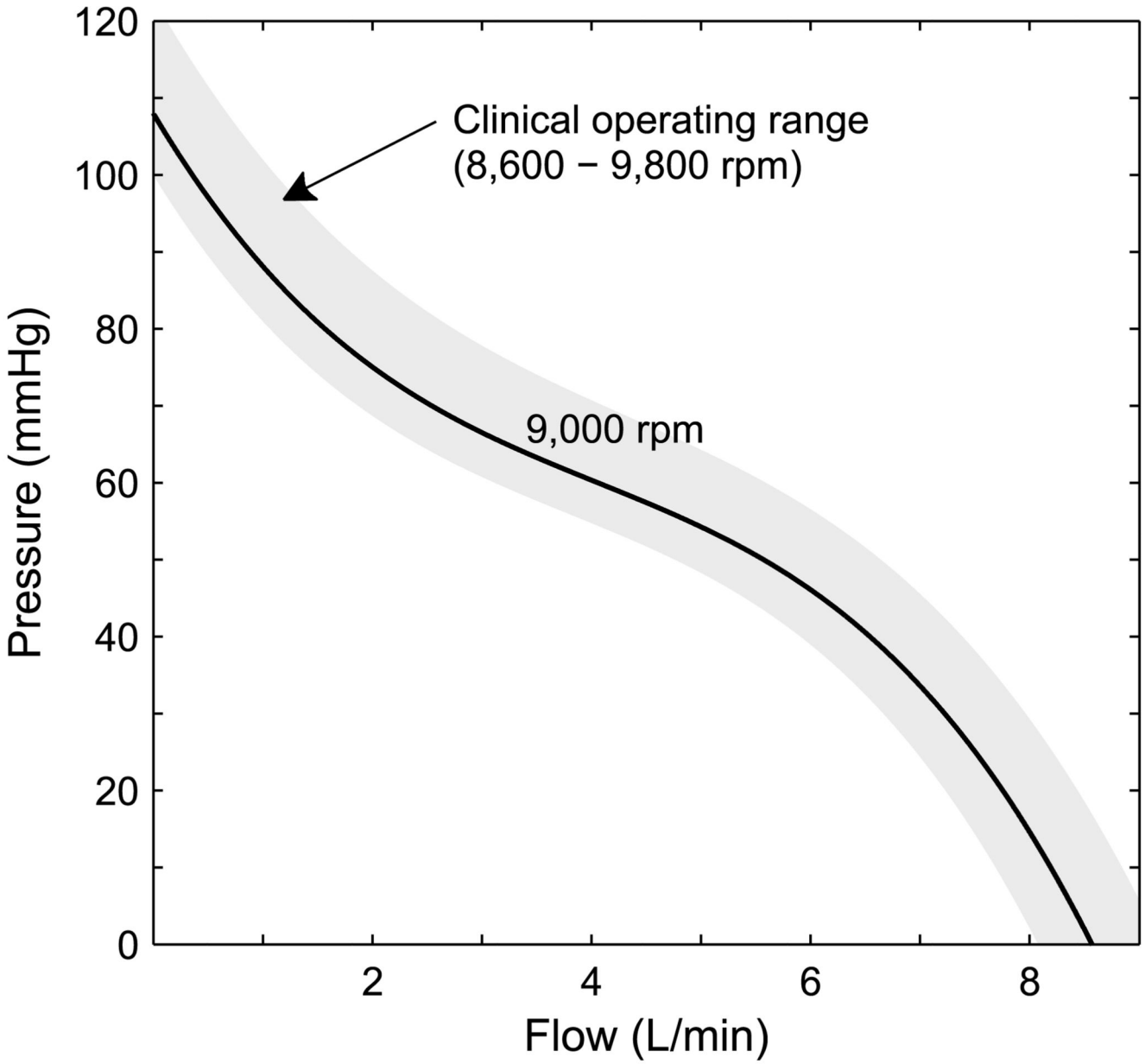

Figure 3.

Pressure-flow curve for the HeartMate II® axial flow pump operated at 9,000 rpm, used to simulate flow in the numerical cardiovascular model of heart failure. The typical clinical operating range of the device is between 8,600 and 9,800 rpm,[43] represented by the shaded region of the plot.

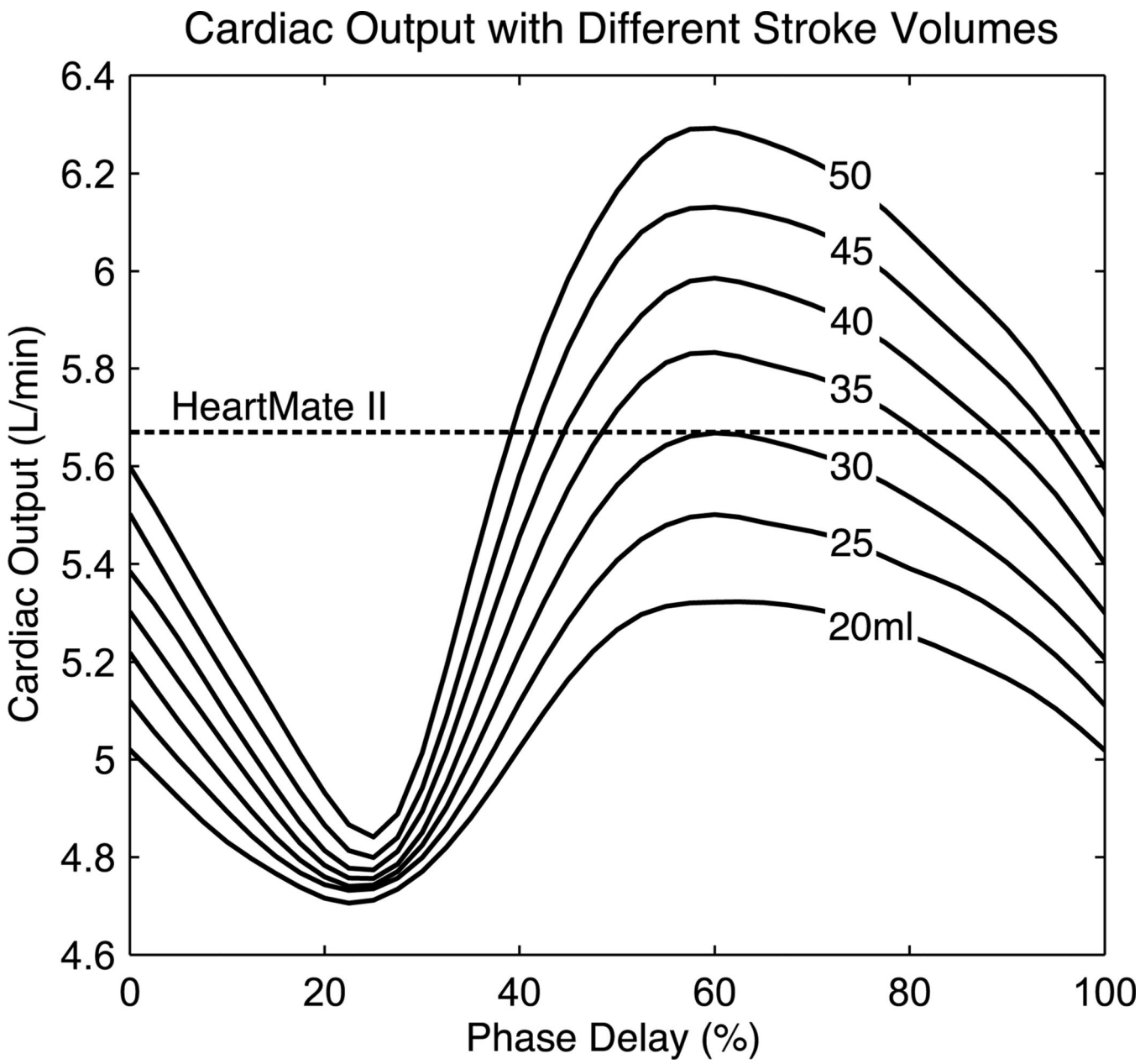

Figure 4.

Cardiac output (CO) versus phase delay (%) with TORVAD™ support at various stroke volumes. The CO when supported with a HeartMate II® continuous flow (CF) is displayed as a dashed line. From this plot, it can be seen that a 30 mL stroke volume TORVAD™ operating with a phase delay of approximately 60% generates an equivalent CO to a CF device. The effect of phasing adjustments and stroke volume changes on CO support levels is also illustrated in this plot.

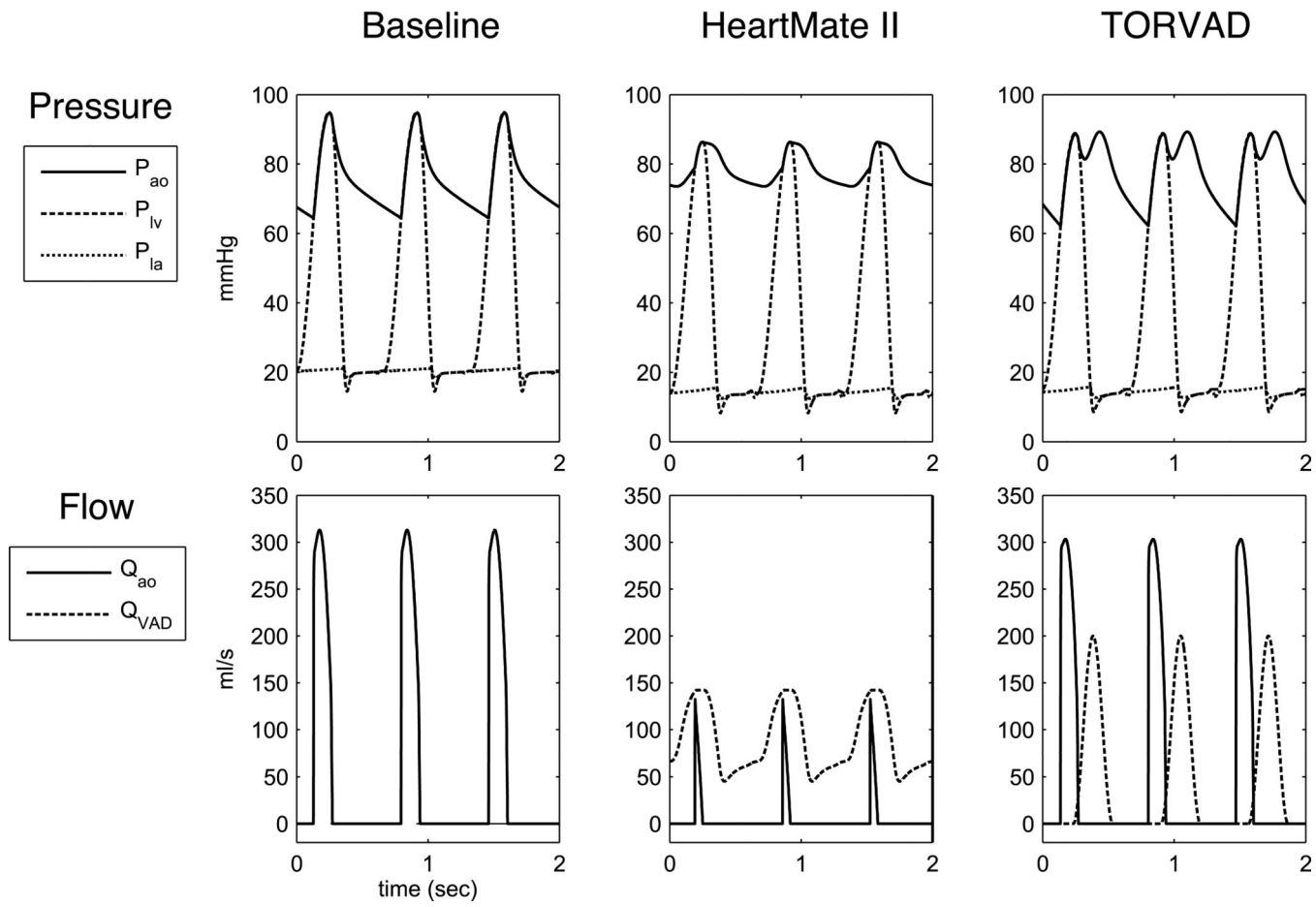

Figure 5.

Hemodynamic pressure (aortic, AOP; left ventricle, LVP; and left atrial, PLA) and flow (aortic valve, Q_{AO}; and VAD, Q_{VAD}) plots for baseline heart failure (HF), HeartMate II® (HMII) support at 9,000 rpm, and TORVAD™ support with a 30 mL early diastolic synchronous counterpulse. With HMII support, aortic valve flow is greatly diminished as blood is shunted through the pump during systole. With TORVAD support™, aortic valve flow is preserved because the pump ejects in early diastole and ceases pumping in systole.

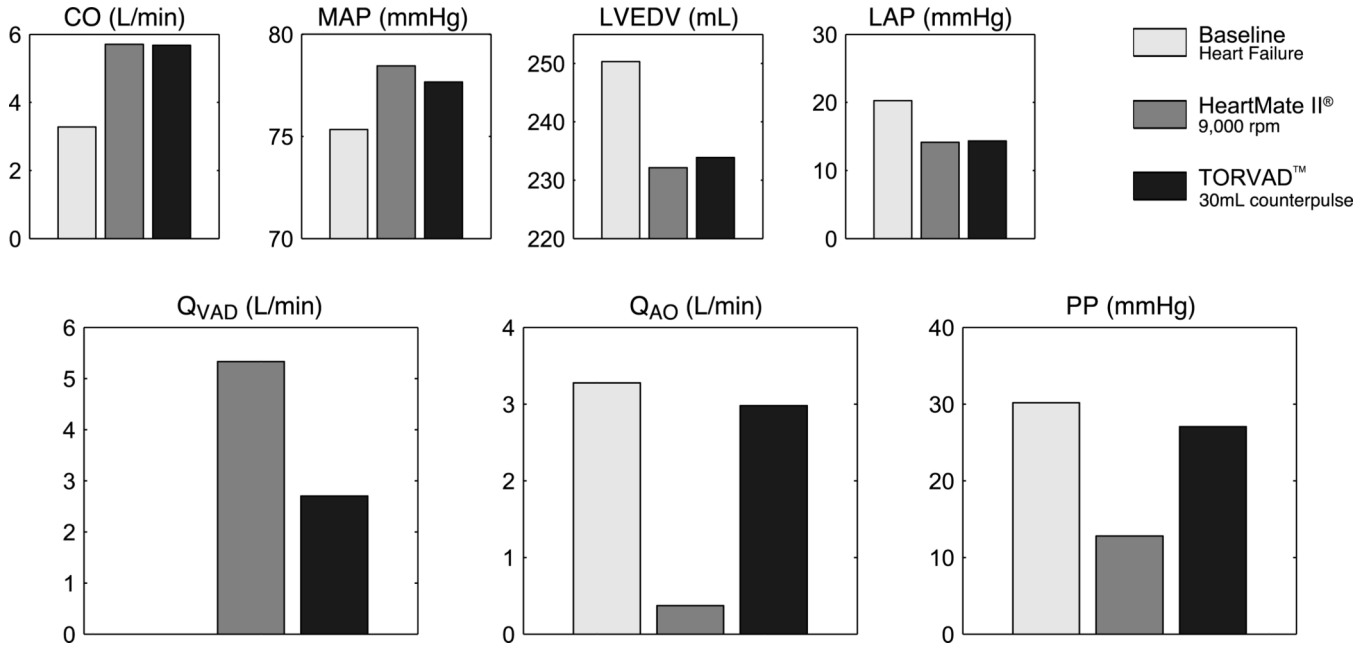

Figure 6.

Bar plots of critical time-averaged hemodynamics. Along the top row, cardiac output (CO), mean arterial pressure (MAP), left ventricular end diastolic volume (LVEDV), and mean left atrial pressure (LAP) are comparably altered with the HeartMate II® (HMII) at 9,000 rpm and the TORVAD™ with a 30ml synchronous counterpulse compared to baseline heart failure (HF). Notable differences in support can be seen along the bottom row of bar plots. The VAD flow rate (Q_{VAD}) is nearly half for the TORVAD™ as compared to the HMII, even with similar cardiac outputs. This difference in VAD flow is made possible by the difference in flow through the aortic valve (Q_{AO}), which is nearly eliminated in the case of HMII support while it is almost entirely maintained in the case of TORVAD™ support. Finally, the last bar plot shows the pulse pressure (PP) calculated by the maximum systolic minus the minimum diastolic pressure. With continuous flow HMII support, the pulse pressure is greatly diminished, while it is almost entirely maintained in the case of TORVAD™ support.

Table 1

Hemodynamic metrics from the computational cardiovascular system model for baseline heart failure, support with the CF HMII, and counterpulse support with a 30 mL TORVAD™.

	HR	CO	Q_{AO}	Q_{VAD}	SP	DP	MAP	PP	LVEDV	LAP
	bpm	L/min	L/min	L/min	mmHg	mmHg	mmHg	mmHg	ml	mmHg
Baseline HF	90	3.1	3.1	0	92.4	63.3	73.7	29.1	244	18.1
HMII 9,000 rpm	90	5.7	0.4	5.3	86.3	73.5	78.5	12.8	232	14.1
TORVAD™ 30 mL CP	90	5.7	3.0	2.7	89.1	62.4	77.7	26.7	234	14.3

Baseline HF = baseline heart failure; HMII = HeartMate II®; TORVAD™ 30 mL CP = TORVAD™ 30 mL early diastolic counterpulse; HR = heart rate; CO = cardiac output; Q_{AO} = flow rate through aortic valve; Q_{VAD} = VAD flow rate; SP = systolic pressure; DP = diastolic pressure; MAP = mean arterial pressure; PP = pulse pressure (SP-DP); LVEDV = left ventricular end-diastolic volume; LAP = mean left atrial pressure.