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High-frequency operation of a pulsatile VAD – a simulation study

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Abstract: Ventricular assist devices (VADs) are mechanical blood pumps that are clinically used to treat severe heart failure. Pulsatile VADs (pVADs) were initially used, but are today in most cases replaced by turbodynamic VADs (tVADs). The major concern with the pVADs is their size, which prohibits full pump body implantation for a majority of patients. A reduction of the necessary stroke volume can be achieved by increasing the stroke frequency, while maintaining the same level of support capability. This reduction in stroke volume in turn offers the possibility to reduce the pump's overall dimensions. We simulated a human cardiovascular system (CVS) supported by a pVAD with three different stroke rates that were equal, two- or threefold the heart rate (HR). The pVAD was additionally synchronized to the HR for better control over the hemodynamics and the ventricular unloading. The simulation results with a HR of 90 bpm showed that a pVAD stroke volume can be reduced by 71%, while maintaining an aortic pulse pressure (PP) of 30 mm Hg, avoiding suction events, reducing the ventricular stroke work (SW) and allowing the aortic valve to open. A reduction by 67% offers the additional possibility to tune the interaction between the pVAD and the CVS. These findings allow a major reduction of the pVAD's body size, while allowing the physician to tune the pVAD according to the patient's needs.

Keywords: hemodynamics with mechanical circulatory support; pulsatile blood pumps; pulsatility; synchronous operation, ventricular assist device (VAD).

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Introduction

Ventricular assist devices (VADs) are mechanical pumps that support the blood circulation in patients with severe heart failure. Originally introduced as support systems that function as a bridge to transplant treatment of the patient, the latest generation of VADs aims rather at becoming an alternative to transplant as a destination therapy [18]. The first generation of VADs introduced in the 1980s were volume displacement pumps. They were driven pneumatically or electromechanically and had mechanical or prosthetic valves [31, 32]. These devices produce a pulsatile flow similar to the one generated by the human heart and are therefore often labeled as pulsatile VADs (pVADs).

The pVADs currently available are mostly operated with a constant stroke frequency, which can be manually changed to adapt the level of support in a range of 60–150 bpm. This means that the stroke frequency is set independently of the heart rate (HR). As early as 1988, Nakamura et al. [24] published comparisons between asynchronous and synchronous operation of pVADs under synchronization ratios that were equal to or lower than the HR. They found the best ventricular unloading in terms of hydraulic stroke work (SW) during asynchronous operation with the stroke frequency in the same range as the patient's HR. This investigation was further assessed by Heredero et al. [14] and Amacher et al. [2], who found that under synchronous operation the timing between ventricle and pump systole has a remarkable impact on the unloading of the left ventricle in terms of hydraulic SW. This influence was not investigated in [24]. Clinical studies with synchronous and asynchronous support have shown comparable outcomes with respect to patient recovery [11] or showed that synchronous support was beneficial with respect to myocardial recovery [20].

The next generation of VADs featured rotary pump designs to produce a continuous blood propulsion either in axial or radial direction (tVAD). Their constant rotary speed results in a reduced aortic pulsatility [30]. The question whether and to what extent pulsatility is required in the human body has been highly disputed since the introduction of turbodynamic VADs (tVADs) [10, 19, 30, 35]. Several studies have compared the ventricular unloading between pulsatile and non-pulsatile VAD support. Garcia et al. [10] found no difference in the level of unloading between pVAD and tVAD support, while Klotz et al. [19] observed a similar degree of left ventricular (LV) pressure unloading but a significantly higher degree of volume unloading with a pVAD [19]. The general consensus is that pulsatile flow offers potential benefits over non-pulsatile flow [29, 30] including increased end organ perfusion [8], better unloading of the LV [23], less risk of right ventricular failure [17], mitigation of aortic valve stenosis and improved vascular remodeling [15], better chances for recovery [20] and reduction of gastrointestinal bleeding [7, 30] when compared with a continuous flow support. Although the mechanics of the last point have not fully been explained yet [28, 29] it is speculated to be linked to the acquired von Willebrand syndrome due to reduced arterial pulsatility when tVADs are employed [7]. The importance of a pulsatile blood flow is also reflected in attempts to augment pulsatility on tVADs by varying the pump speed for the newer generation of VADs such as the HeartMate III (St. Jude Medical, Inc., St. Paul, MN, USA). Several groups have published studies about speed modulation for tVADs currently available and in development [5, 9, 23], as well as algorithms designed to restore some form of pulsatile flow [16].

Over the last decade, despite these potential benefits of pulsatile flow, the number of implanted pVADs has declined, whereas the number of tVAD implantations has greatly increased [18]. Besides concerns of thrombus formation inside the pump cavity and mechanical longevity, the main drawback of pVADs is their physical size and weight which preclude or greatly compromise their implantation for the majority of patients. The resulting paracorporeal usage presents a high risk of infection [32] as well as a physical and psychological burden for the recipients. The size of the pVAD is closely linked to the required stroke volume, which in turn is determined by the demanded pump flow and stroke rate. We propose a reduction of the stroke volume to increase the feasibility of full pVAD implantation while maintaining the pVAD's support capability by increasing the pump's stroke rate. Before extensively designing a device we studied the interaction of the human cardiovascular system (CVS) and the pVAD under various operation modes using numerical simulations to assess the feasibility of a high-frequency operation.

In our study we present numerical simulation results of the interaction of the CVS with a pVAD under synchronous operation with stroke frequencies that are either equal to the HR or multiples by a factor of two or three. With this investigation we assessed the feasibility of high frequency operation of pVADs and the corresponding reduction of the stroke volume and the ultimate pump size. Our results suggest that a pVAD support with stroke rates up to three times the HR can reduce the stroke volume to 29% of the original volume, which corresponds to an estimated reduction of the pump's body size to 40%. The negative hemodynamic effects of this high frequency operation can be reduced by choosing suitable pump parameters that allow adjustment of the interaction between the pVAD and the CVS.

Materials and methods

For the simulations we used a numerical model of the human CVS established by Colacino et al. [6] with an added suction emulation proposed by Ochsner et al. [25]. The former model was developed to study the interaction of the human CVS with a pVAD and includes

Table 1: Overview of pump parameters used for the simulations.

Settings	Stroke frequency (f_{st})	Phase shift (φ_p)	Systolic fraction (φ_p)
#01	Equal to heart rate	0%	20, 25, 30, …, 80%
#02		2%	20, 25, 30, …, 80%
#03		4%	20, 25, 30, …, 80%
		⋮	
#46		90%	20, 25, 30, …, 80%
#47	Two times heart rate	0%	20, 25, 30, …, 80%
#48		2%	20, 25, 30, …, 80%
#49		4%	20, 25, 30, …, 80%
		⋮	
#92		90%	20, 25, 30, …, 80%
#83	Three times heart rate	0%	20, 25, 30, …, 80%
#84		2%	20, 25, 30, …, 80%
#85		4%	20, 25, 30, …, 80%
		⋮	
#138		90%	20, 25, 30, …, 80%

both the systemic and the pulmonary circulation as well as both atria and ventricles. The atria and ventricles are modeled as non-linear time-varying elastances which provide active contraction. The contractility level of the LV was set to 34% of the physiological value according to [6] to represent the pathological case. We augmented the CVS model with a numerical pVAD with ventriculo-aortic cannulation. No dynamic effects of the pump nor the fluid were included as we aimed to investigate solely the interaction between the pump flow and the CVS independent of any given pump design and actuation method. Our generic pump model was implemented directly as either a sinusoidal- or a square-wave-flow profile, both parameterized with the stroke volume V_{st}, the stroke frequency f_{st}, the phase shift φ, and the systolic fraction φ_p. The latter three were chosen manually with the different combinations of settings shown in Table 1.

Figure 1 shows the definition of the phase shift φ introduced by [1]. φ is the time delay between the R-wave peak of the electrocardiogram (ECG) signal and the middle of the pump systole in relation to the duration of one cardiac cycle. During the 2:1 synchronization ratio, the second pump cycle has an additional 50% phase shift. In the case of φ=25%, the second pump systole would occur at φ=75%, as shown in Figure 1. For the 2:1 synchronization ratio, the intervals $\varphi \in [0\ldots50\%]$ and $\varphi \in [50\ldots100\%]$ therefore yield the same results. The same line of reasoning can be applied to the 3:1 synchronization ratio. Hence the results in the Figures 2–6 are only plotted up to φ=50% for the 2:1 synchronization ratio and φ=33% for the 3:1 ratio, respectively.

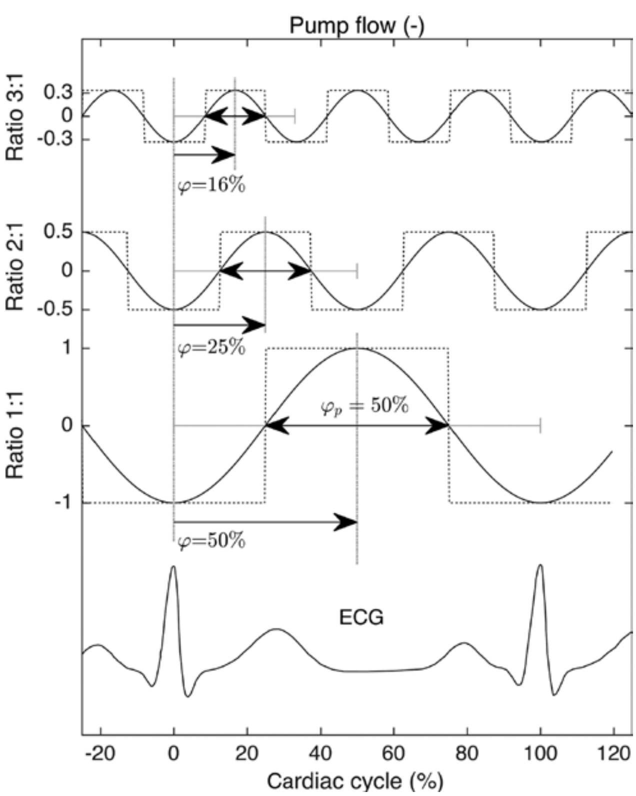

Figure 1: Definition of the phase shift (φ) and the systolic fraction (φ_p).
The upper three plots show the pump flow, where the black lines represent a sinusoidal (solid line) and a square (dotted line) pump flow profile, respectively, for three different synchronization ratios. Negative values represent the pump's diastole and positive numbers represent the pump's systole. The bottom plot illustrates an electrocardiogram (ECG), with the large peak at 0% representing the R-wave.

Figure 1 also shows the definition of the systolic fraction φ_p, which was varied independently and is calculated as the duration of pump systole in relation to the duration of one pump cycle. Figure 1 shows φ_p=50% for the synchronization ratios 1:1, 2:1 and 3:1. In our simulations we varied φ_p only between 20% and 80% in order to avoid high peak flows during short systole or diastole, respectively.

In order to achieve a steady state from cycle to cycle, the stroke frequency (f_{st}) was synchronized with the simulated HR because asynchronous operation yields beat-to-beat variations in the hemodynamic signals. In our simulations we investigated stroke frequencies that were equal to or, twice or three times the HR – in the following designated as synchronization ratios (1:1, 2:1, 3:1).

The VADs V_{st} was dynamically adapted in all cases by a proportional-integral (PI) controller to achieve a constant total cardiac output (tCO) of 5 l/min, as this value is often mentioned as a minimal requirement by physicians and in literature alike [13].

The transfer function of this controller is given by:

$$C(s)=k_p\cdot\left(1+\frac{1}{T_i\cdot s}\right) \tag{1}$$

where k_p=0.75 is the proportional gain and T_i=2 s is the integrator time constant. We chose to keep the tCO (sum of blood flow through VAD and aortic valve) constant to ensure a comparability between the different pump settings. As soon as steady-state was reached, one cardiac cycle was saved for subsequent analysis.

The assist ratio is the relation of flow through the VAD compared to the tCO. The chosen pump parameters influence the assist ratio as we automatically adapted the V_{st}. To minimize the V_{st} the pump parameters that maximize the blood flow through the aortic valve (q_{av}) have to be found since the necessary stroke volume can be calculated as the difference between the target tCO of 5 l/min and the q_{av} divided by the stroke frequency (f_{st}):

$$V_{st}=\frac{\text{tCO-}q_{av}}{f_{st}} \tag{2}$$

For a baseline comparison, we simulated the CVS without VAD support and with a tVAD running at a constant speed. The flow through the tVAD q_{cVAD} was modeled by applying the numerical model of the Heartware HVAD published by Granegger et al. [12]. The pressure flow relation through the tVAD is given as:

$$p_{ao}\text{-}p_{LV}=a\cdot\omega^2\text{-}b\cdot q_{cVAD}\text{-}L\cdot\frac{dq_{cVAD}}{dt} \tag{3}$$

where p_{ao} represents the aortic pressure, p_{LV} the pressure in the LV and ω the rotational speed, which was adjusted by a PI controller (k_p=1,T_i=0.5 s) to yield the same tCO of 5 l/min as in the pVAD simulations. The model parameters were taken from [12] and are $a=1.29\cdot10^{-3}$ mm Hg·s², $b=3.94\cdot10^{-3}$ mm Hg·s²/ml² and L=0.02 mm Hg·s²/ml.

For our analysis, we considered the left ventricular stroke work (LVSW), the mean blood flow through the aortic valve, the occurrence of suction events, and aortic pulsatility. The LVSW was calculated as:

$$SW_{LV}=133.3\cdot10^{-5}\int p_{LV}\cdot(q_{av}+q_{bpin}\text{-}q_{mv})dt \tag{4}$$

where q_{av}, q_{bpin} and q_{mv} represent the blood flow through the aortic valve, the flow from the ventricle into the bypass (pVAD) and the

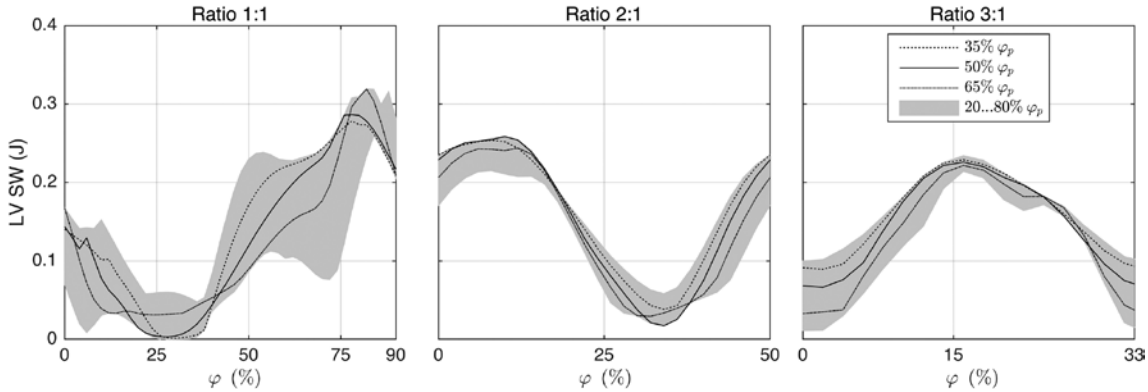

Figure 2: Left ventricular stroke work (LVSW) given as hydraulic energy produced during one cardiac cycle vs. the phase shift (φ). The different lines illustrate different systolic fractions (φ_p) exemplarily, while the gray area shows the full range of reachable values.

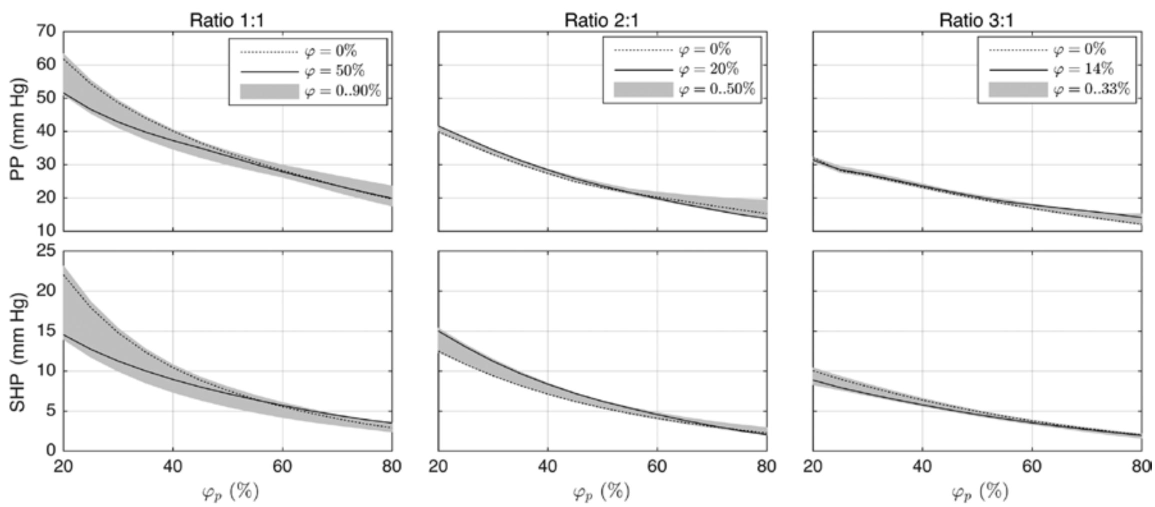

Figure 3: Aortic pulse pressure (PP) and surplus hemodynamic pressure (SHP) vs. the systolic fraction (φ_p) for synchronization ratios 1:1, 2:1 and 3:1.
The different lines illustrate different phase shifts (φ) exemplarily, while the gray area shows the full range of reachable values.

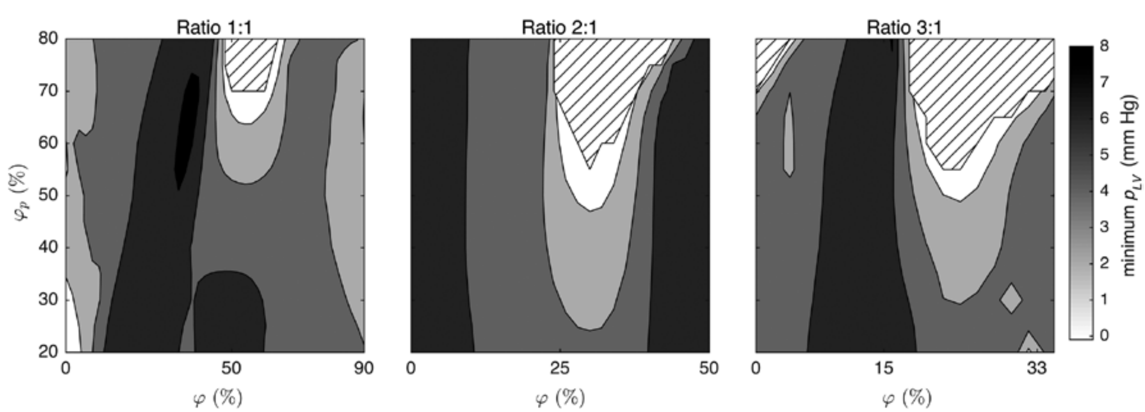

Figure 4: Minimum pressure in the LV during one cardiac cycle for the synchronization ratios 1:1, 2:1 and 3:1.
The x- and y-axes illustrate the phase shift (φ) and systolic fraction (φ_p) of the pump, respectively. The hatched area indicates operation parameters that lead to ventricular suction.

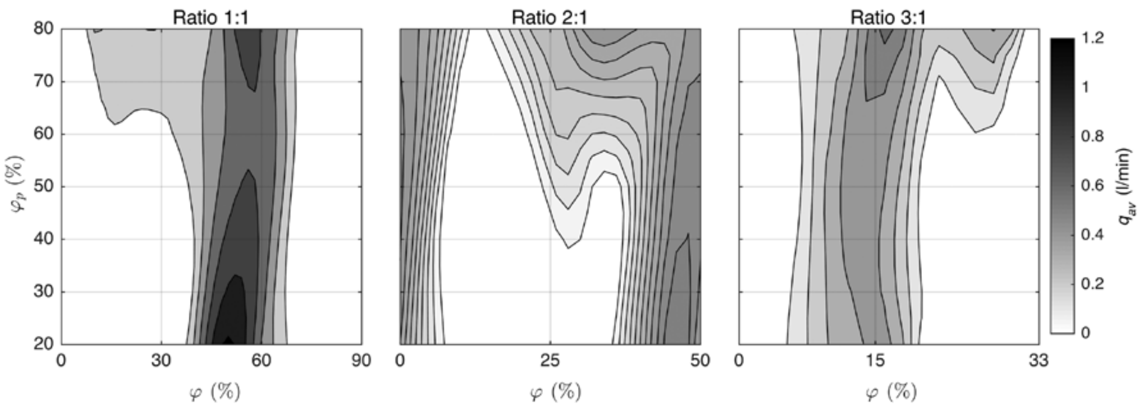

Figure 5: Blood flow through aortic valve (q_{av}) during pVAD support.
The x- and y-axes illustrate the phase shift (φ) and systolic fraction (φ_p) of the pump, respectively, while the color reference on the right indicates the amount of blood flow through the aortic valve.

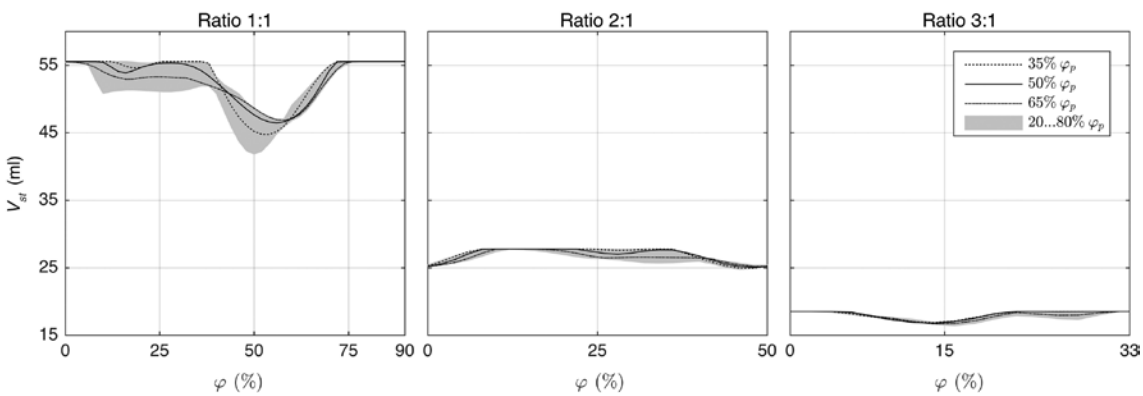

Figure 6: Necessary stroke volume (V_{st}) of pVAD in order to achieve a total cardiac output (tCO) of 5 l/min vs. the phase shift (φ).
The different lines illustrate different systolic fractions (φ_p) exemplarily, while the gray area shows the full range of reachable values.

mitral valve, respectively. To assess the risk of suction events we recorded the minimum pressure in the LV. The inclusion of the suction emulation by [25] causes the p_{LV} to be negative when suction occurs. Aortic pulsatility was calculated as aortic pulse pressure (PP) and the surplus hemodynamic pressure (SHP) was calculated according to the definition given in [30], with q_{bpout} representing the flow from the bypass (pVAD) into the aorta.

$$PP=\max(p_{ao})\text{-}\min(p_{ao}) \tag{5}$$

$$\mathrm{SHP}=\frac{\int\left(q_{av}+q_{bpout}\right)\cdot p_{ao}\cdot dt}{\int\left(q_{av}+q_{bpout}\right)\cdot dt}\text{-mean}(p_{ao}) \tag{6}$$

Results

Table 2 lists the results of the numerical simulations using the sinusoidal-flow profile and the square-flow profile, as well as the results obtained with the simulated tVAD and an unsupported CVS for comparison, each with HRs of 70, 90, and 110 bpm. The presented maximum q_{av}, minimum p_{ao}, maximum PP, maximum SHP, minimum and maximum LVSW are in each case computed over all the pump settings φ, φ_p listed in Table 1.

Figures 2–7 show the results of our simulations with sinus-flow profile and HR=90 bpm.

Figure 7 shows the p_{LV} and the p_{ao} for co- and counterpulsation during one cardiac cycle for the synchronization ratios 1:1, 2:1 and 3:1. Copulsation represents the pump setting that minimizes the LVSW, whereas counterpulsation represents maximum LV loading (compare Figure 2). The number of pulses in the aortic pressure increases according to the pVAD synchronization ratio. The thin lines illustrate p_{ao} and p_{LV} during copulsation mode, whereas the thick lines denote a counterpulsation mode. Due to the more frequent flow from the pVAD into the aorta, the diastolic arterial pressure is elevated from 84 mm Hg to 89 mm Hg and 91 mm Hg for the 2:1 and 3:1 ratios, respectively. At the same time, the PP for the three

Table 2: Simulation overview showing the maximum blood flow through the aortic valve (max q_{av}), minimum diastolic aortic pressure (min p_{ao}), maximum aortic pulse pressure (max PP), maximum surplus hemodynamic pressure (max SHP), minimum stroke work (min SW) and maximum left ventricular stroke work (max SW) for the supported ventricle.

Simulation settings	HR (bpm)	tCO (l/min)	Ratio	max q_{av} (l/min)	min p_{ao} (mm Hg)	max PP (mm Hg)	max SHP (mm Hg)	min SW (J)	max SW (J)
pVAD, sinusoidal flow	70	5.0	1:1	0.89	74	72	26	0.00	0.35
			2:1	0.18	84	50	18	0.00	0.31
			3:1	0.25	87	37	13	0.00	0.25
	90	5.0	1:1	1.23	78	63	23	0.00	0.32
			2:1	0.54	86	42	15	0.02	0.26
			3:1	0.64	88	32	10	0.00	0.24
	110	5.0	1:1	1.58	80	57	21	0.00	0.30
			2:1	0.59	88	36	13	0.02	0.21
			3:1	1.03	89	29	9	0.00	0.24
pVAD, square flow	70	5.0	1:1	0.87	73	70	20	0.00	0.41
			2:1	0.21	84	48	16	0.00	0.31
			3:1	0.40	86	42	13	0.00	0.28
	90	5.0	1:1	0.89	78	59	18	0.00	0.39
			2:1	0.58	86	42	14	0.02	0.29
			3:1	0.47	85	40	11	0.00	0.23
	110	5.0	1:1	1.34	80	54	17	0.00	0.32
			2:1	0.54	87	39	13	0.03	0.21
			3:1	1.00	82	44	10	0.00	0.24
tVAD, constant speed	70	5.0	–	0.00	95	13	1	0.28	n.a.
	90		–	0.00	95	12	1	0.25	n.a.
	110		–	0.00	96	11	1	0.21	n.a.
Without VAD support	70	3.4	–	3.44	64	42	11	0.48	n.a.
	90	3.5	–	3.50	68	38	11	0.38	n.a.
	110	3.5	–	3.55	70	34	10	0.32	n.a.

For the assistance of different ventricular assist device (VAD) models the different flow profiles, synchronization ratios and heart rates (HRs) are specified. The maxima and minima of the presented quantities are calculated over all phase shifts (φ) and systolic fractions (φ_p). The gray rows represent the results shown in Figures 2–7.

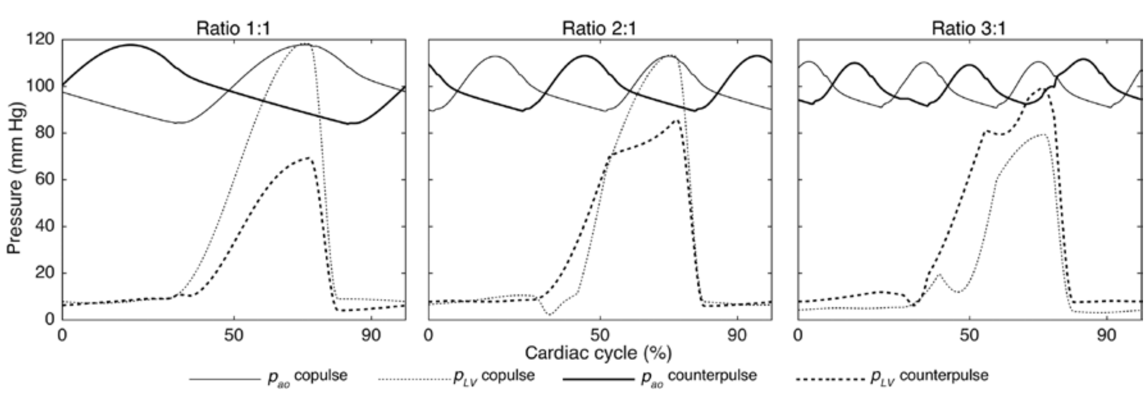

Figure 7: Left ventricular (p_{LV}) and aortic pressure (p_{ao}) for synchronization ratios 1:1, 2:1 and 3:1 in co- and counterpulsation mode. Co- and counterpulsation represent maximum and minimum left ventricular unloading, respectively. The number of pressure peaks in p_{ao} corresponds to the number of pVAD systole during one cardiac cycle.

cases reduces from 30 mm Hg to 21 mm Hg and 17 mm Hg, respectively.

For the synchronization ratios 2:1 and 3:1 the number of pump cycles increase, while the total pVAD flow remains constant. As a result, the V_{st} reduces and the flow becomes more continuous. Thus, the influence of the pump timing on the LV decreases. Figure 7 shows that the difference between the systolic p_{LV} for co- and counterpulsation reduces as the synchronization ratio is increased from 1:1 to 2:1 and 3:1.

Ventricular unloading is a necessity for any type of VAD. Figure 2 shows the LVSW vs. phase shift (φ) that resulted for all three synchronization ratios analyzed. Complete unloading of the ventricle was achieved with co-pulsation, when the pVAD was operated with φ=28% during 1:1 synchronization, φ=34% for the 2:1 ratio and φ=3% for the 3:1 ratio. Maximum loading of the LV occurred with counterpulsation, which was reached under φ=78% during 1:1 synchronization (0.32 J), φ=10% for 2:1 (0.26 J) and φ=16% for 3:1 (0.24 J). The gray area illustrates the range of LVSW values that can be achieved for a given value of φ and synchronization ratio by changing φ_p, e.g. for a 1:1 ratio and φ=50% the LVSW varies between 0.1 J for φ_p=35% and 0.23 J for φ_p=20%. For all three synchronization ratios the pVAD is capable of reducing the LVSW compared to the unsupported case, during which the LV is only able to produce 3.4 l/min of tCO while requiring 0.38 J of LVSW every cycle. With the assistance of a tVAD this hydraulic energy is reduced to 0.25 J (see Table 2).

The sustainment of aortic pulsatilty is a major advantage of pVADs compared to tVADs. Figure 3 shows that the maximum achievable PP reduces with the two synchronization ratios 2:1 and 3:1 (also compare Figure 7). The maximum PP reduces from 63 mm Hg during 1:1 synchronization to 42 mm Hg and 32 mm Hg for the 2:1 and 3:1 synchronization, respectively. Figure 3 also shows the dependence of PP on the φ_p with the PP reducing for an increasing φ_p. The gray area illustrates the range of PP that can be achieved for a given value of φ_p, when φ is varied, e.g. for φ_p=40% and 1:1 synchronization the PP ranges from 35 mm Hg for φ=62% to 41 mm Hg for φ=90%.

The same trends are depicted in the bottom row of Figure 3 for the SHP. In the unsupported case the pathological CVS creates an SHP of 11 mm Hg due to the low tCO of only 3.4 l/min, whereas in the case of a tVAD support this value drops to 1 mm Hg (see Table 2).

During VAD support suction events have to be avoided in order to prevent damaging the ventricle. Figure 4 shows the minimum pressure observed in the LV during one cardiac cycle for the full range of pVAD settings (Table 1). The minimum LV pressure (p_{LV}) is depicted according to the color bar on the right side. Hatched areas indicate pump parameters where the p_{LV} drops to 0 or below. This occurs for various phase shifts (φ), when φ_p>65% during 1:1 synchronization, φ_p>50% for the 2:1 ratio and φ_p>45% for the 3:1 synchronization ratio. When φ_p>50%, the pump diastole becomes shorter than the systole. Thus the same amount of blood is sucked out of the LV in a shorter time and the likelihood for suction increases.

Figure 5 shows the blood flow through the aortic valve (q_{av}) for the full range of pump settings defined in Table 1. The value of q_{av} (1.2 l/min) is reduced compared to the case without VAD support (3.4 l/min) due to the reduced blood volume remaining in the LV. The flow values shown are averaged over one cardiac cycle. The darker areas indicate higher values of q_{av} according to the color bar given on the right edge of Figure 5. White areas illustrate pump parameters where the aortic valve remains closed. The maximum q_{av}=1.2 l/min is reached when the pVAD is operated with 1:1 synchronization, φ=50% and φ_p=20%. The maximum q_{av} is reduced to 0.54 l/min for the 2:1 synchronization and 0.64 l/min for 3:1 synchronization, respectively. In the baseline simulation with tVAD support the aortic valve remained shut (see Table 2).

Figure 6 shows the necessary stroke volume (V_{st}) that resulted from the q_{av} shown in Figure 5 and Equation 2. The V_{st} is plotted against φ, while the different lines and the gray area illustrate the range of V_{st} that can be achieved for a given value of φ and synchronization ratio by changing φ_p. When the aortic valve remains closed during 1:1 synchronization (e.g. φ=80%, see Figure 5) the necessary V_{st} to achieve a tCO of 5 l/min is 55.6 ml. This value is reduced to 50% when the 2:1 synchronization ratio is used (e.g. φ=12%), and to 33% for the 3:1 ratio (e.g. φ=0%). The V_{st} can be further reduced by setting the pump parameters to maximize q_{av}. The lowest required V_{st}=41.9 ml during 1:1 synchronization can be achieved by setting φ=50% and φ_p=20%. For the 2:1 synchronization V_{st} can be reduced to 24.8 ml (φ=46%, φ_p=20%) and to 16.4 ml (φ=16%, φ_p=80%) for the 3:1 synchronization (see Figures 5 and 6).

Discussion

We simulated the hemodynamic effects of a cardiac-cycle synchronized pVAD with synchronization ratios that are multiples of the HR to obtain more knowledge about the interaction of a pVAD with the human CVS and to assess the feasibility of a chamber size reduction of pVADs. Previous studies have investigated synchronization ratios (1:2 and 1:4) lower than the HR under one given phase-shift setting [24] with the intention of establishing a weaning protocol. The importance of considering the pump timing and systolic fraction as an integral part of the investigation has been shown *in vivo* by [2] for pVADs and by [1, 3, 4, 26, 33, 34] both in silico and *in vivo* for tVADs.

We compared our results with simulations including a constant-speed tVAD. The tVAD simulation was intended as a baseline experiment that represents the use of tVADs in clinical application today. There are numerous studies that have investigated augmented pulsatility in tVADs through speed modulation [1, 3, 4, 16, 26, 27, 33, 34]. These studies have shown improved levels of pulsatility, left ventricular unloading and blood flow through the aortic valve, but were exceeded by the values of our pVAD simulation. A reduction of the pVAD size to a full implantable volume and shape would therefore present a major improvement.

In our simulations we found no remarkable differences between sinus- and square-flow profiles. There were small differences between the flow profiles in regards to the hemodynamics (see Table 2). These differences, however, were negligible compared to the effects of the three pump parameters φ, φ_p and synchronization ratio. These findings agree with the results published by Pirbodaghi et al. [26], who investigated different speed modulation patterns for tVADs. In our investigations the intensity of hemodynamic effects attributed to both simulated VADs (pVAD and tVAD) scales with the assist ratio. For an increased ventricular activity, e.g. tachycardia (110 bpm), the blood flow through the VAD decreased and the hemodynamic effects introduced by both VADs diminished. For example, as less blood flowed through the pVAD, the difference between maximum and minimum LV unloading reduced from 0.35 J for an HR of 70 bpm to 0.30 J for 110 bpm, while the maximum achievable PP reduced from 72 mm Hg to 57 mm Hg. These results match the observations by Lim et al. [21], who studied the interaction between tVADs and the CVS under exercise conditions and found the tCO to be closely linked to the HR.

The capability to unload the LV is a necessity for any VAD. In our investigation, the LVSW varied between 0 and 0.35 J per cardiac cycle in the range of $\varphi \in [0\ldots90\%]$. The phase shift that yielded the biggest unloading of the LV changed when higher synchronization ratios were used (φ=28% for 1:1 ratio, φ=34% for 2:1, φ=3% for 3:1). Figure 3 shows that for synchronization ratios of 2:1 and 3:1 the LVSW depends on φ to a similar extent as in the 1:1 case. In all operation modes both the pVAD and the tVAD greatly reduced the ventricular SW and increased perfusion compared to the non-assisted case (Table 2). However, for the pVAD, parameters could be found for all three synchronization ratios that reduced the LVSW below 0.02 J, while for the constant speed tVAD the LVSW remained at 0.21 J for the same tCO.

While the LVSW mainly depends on φ, it can be observed in Figure 4 that the risk of suction primarily occurs for φ_p>50% when the pVAD diastole is shorter than the pVAD systole. For a given V_{st}, the shorter diastole causes a higher peak flow into the pVAD, which explains the higher tendency for ventricular suction. The reduction of the risk of ventricular suction by employing only low systolic fractions offers the additional advantage of increasing the aortic pulsatility. Figure 2 shows two measures for the aortic pulsatility, namely PP and SHP. Both measures show a level of aortic pulsatility exceeding that of a tVAD support, which yielded a diminished PP of 12 mm Hg. In the cases of a 2:1 and a 3:1 synchronization ratio the pump ejects blood multiple times during the LV diastole thus increasing p_{ao} during the diastolic phase of the cardiac cycle. Our simulations also show that both PP and SHP decrease with an increasing systolic fraction φ_p as the same amount of blood is ejected into the aorta over a longer period of time, thus causing a lower peak flow. While the maximum pulsatility diminishes with higher synchronization ratios, φ_p can be varied to achieve a desired level of aortic pulsatility.

The ability to at least partially open the aortic valve is an important factor for preventing aortic valve insufficiency in VAD patients [22]. Figure 5 shows that in our simulations pump settings exist for all three synchronization ratios where the aortic valve opens. Similarly to the LVSW, the blood flow through the aortic valve q_{av} depends on φ. More noticeably, the φ that yielded the highest q_{av} was not equal to the φ causing the highest loading of the LV, e.g. during the 1:1 synchronization the maximum q_{av}=1.2 l/min was reached with φ=50%, while the maximum LVSW was reached with φ=78% (see Figure 3). For all three synchronization ratios, φ can be varied to achieve a partial opening of the aortic valve. This represents an improvement over our baseline simulation with a constant-speed tVAD support during which the aortic valve remained shut for the entire time.

The flow through the aortic valve also needs to be considered for the reduction of the pVAD's stroke volume V_{st}. The aim of our study was to investigate how the V_{st} could be reduced. With the incorporation of synchronization ratios 2:1 and 3:1, the necessary V_{st} when the aortic valve remained closed could be reduced to 50% or 33% of the original V_{st}, respectively. By choosing pVAD parameters that maximize the blood flow through the aortic valve q_{av}, the V_{st} can be further reduced. In our simulations, the smallest V_{st}=16 ml was found for φ=16%, φ_p=80% and a 3:1 synchronization ratio (see Figures 5 and 6). This represents a reduction of V_{st} to 29% of the original 55 ml required during operation with a 1:1 synchronization. A V_{st} value of 16 ml also represents a volume reduction to 88% of the V_{st} with a closed aortic valve during a 3:1 synchronization. For all three synchronization ratios the V_{st} reduced to <90% of its original volume if the pump parameters are chosen to minimize the V_{st}. It is therefore of crucial importance to synchronize the pVAD in order to achieve a maximum downsizing for full implantability of a pVAD. Alternatively, a V_{st} reduction to 33% of the original volume allows the other pump parameters φ, φ_p to be tuned to achieve a better unloading of the ventricle or a higher aortic PP, for instance.

For this study, we limited the synchronization ratio to a maximum of 3:1, since for higher ratios the PP would reduce below 30 mm Hg which is the level that has been achieved by a tVAD with augmented pulsatility [1]. Arguably, one could potentially further increase the synchronization ratio. However, the load on mechanical components would increase and dynamic effects induced by pump's valves and fluid inertia would increase the percentage of backflow through the closing valve and limit the flow velocity gradients. Thus, it cannot be assumed that stroke volume V_{st} decreases linearly with the synchronization ratio and that the necessary V_{st} will indeed be larger than calculated. Furthermore, the flow would become more and more continuous, which is especially critical as the beating heart in such a pump would not be able to induce pulsatility to the arterial flow when the aortic valve is closed, as opposed to the tVAD case where no valves are present. Furthermore, it remains to be investigated to what extent the model used in our simulations is valid for high frequency VAD operation as the underlying dynamics and parameters have not been validated for stroke frequencies beyond physiological range. To what extent the V_{st} reduction presented in this text can be translated into pVAD body size reduction remains under investigation.

Conclusion

Synchronization ratios higher than one represent a variable that has not been analyzed yet for the control of the interaction between the pVAD and the CVS. We propose pVAD stroke rates that exceed the HR and thereby enable the reduction of its stroke volume to increase the feasibility of full pVAD implantability. Our results show that the stroke volume of a simulated synchronized pVAD can be reduced to 29% of its original volume by using a 3:1 synchronization ratio, φ=16% and φ_p=20%. During this operation, no suction occurs, the aortic valve opens during systole, the aortic PP is kept at 31 mm Hg while the LVSW is reduced by 28% compared to the unsupported pathological case. Alternatively, a stroke volume reduction to 33% of the original volume allows the other pVAD parameters φ and φ_p to be tuned for an increased unloading of the left ventricle or an increased aortic PP. These findings allow a major reduction of the pVAD's body size, while allowing the physician to tune the pVAD according to the patient's needs.

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