Article

Computational Evaluation of Cardiac Function in Children Supported with Heartware VAD, HeartMate 2 and HeartMate 3 Left Ventricular Assist Devices

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Abstract: Heart failure is one of the principal causes of morbidity and mortality in children. Treatment techniques may not work, and heart transplantation may be required as a result. The current state of donor-organ supply means that many patients cannot undergo transplantation. In these patients, ventricular assist devices (VADs) may be used to bridge the time until the transplantation. Continuous-flow VADs are increasingly being implanted to paediatric patients. The aim of this study was to evaluate cardiac function in children supported with Heartware HVAD, HeartMate2 and HeartMate3 devices using computational simulations. A lumped-parameter model simulating cardiac function in children around 12 years of age was used to simulate dilated cardiomyopathy and heart-pump support. The operating speeds in HVAD, HeartMate2 and HeartMate3 were selected as 2600 rpm, 8700 rpm and 5200 rpm constant speed, respectively, while the Lavare cycle and artificial-pulse modes were used to generate mean pump outputs at around 4.40 L/min and mean arterial pressures at around 82 mmHg in each device. Aortic pulse pressure was 11 mmHg, 14 mmHg and 6 mmHg under HVAD, HeartMate2 and HeartMate3 support, respectively. HVAD's Lavare cycle and HeartMate3's artificial pulse increased aortic pulse pressure to 15 mmHg and 20 mmHg. HeartMate3 with artificial-pulse mode may be more beneficial in reducing arterial-pulsatility-associated problems.

Keywords: continuous-flow left ventricular assist device; paediatrics; dilated cardiomyopathy; computational modelling

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1. Introduction

Heart failure is one of the main causes of morbidity and mortality in children [1]. Various causes such as cardiomyopathies, congenital malformations and anthracycline toxicity may result in reduced cardiac output in children [2]. Heart failure due to cardiomyopathy affects approximately 27% of paediatric heart failure patients [3], whereas the mortality rate in dilated cardiomyopathy (DCM) reaches up to 21% for the first year of life [4]. Medical management of DCM begins with pharmacological therapy [5]; however, only 66% to 70% of paediatric patients are suitable for this drug approach [5]. The evidence in adults shows that the long-term effects of drugs may worsen myocardial damage, thus increasing the severity of heart failure [5,6]. Moreover, the causes of cardiomyopathy may vary significantly; in some cases, drug therapy, including diuretics, beta-blockers or digoxin, may not work and heart transplantation would be required. However, the current state of donor-organ supply means that many patients are not treated, or transplants are delayed, due to the lack of suitable donor organs. In these patients, ventricular assist devices (VADs) may be used to bridge the time between the decision to transplant and the actual transplantation [7].

The selection of VAD type is primarily dependent on the patient's body size, with the suggested lower limit for continuous-flow VAD implantation being around 0.6 m²

body surface area [8]. Experiences of using different continuous-flow VADs in children have mainly been reported for the following three devices: the HeartMate 2 (HM2) device (Thoratec, Pleasanton, CA, USA), which is a suitable option for children with a body surface area over 1.3 m² [7]; the Heartmate 3 (HM3) ventricular assist device (Thoratec, Pleasanton, CA, USA), which is a centrifugal pump and can be used in patients with 0.8 m² body surface area [9]; and the HeartWare HVAD continuous-flow device (HeartWare, HeartWare Systems, Framingham, MA, USA), which can be used in patients with a BSA under 1.0 m² [10].

Current challenges in continuous-flow VAD support in children include patient selection, the influence of risk profiles, small body sizes for continuous-flow VADs, surgical modifications to mitigate patient–device size mismatch, and selection of the most suitable device for each patient considering these factors [11–13]. A lack of data in children under VAD support poses further challenges in treating paediatric patients; hence, health centres implant continuous VADs to children using data from adults [11]. Moreover, HVAD and HM3 devices have modes with variable operating speeds such as the Lavare cycle and artificial pulse; however, studies focusing on these features consider mechanical circulatory support in adults [14]. A direct comparison of the haemodynamic outcome during continuous-flow VAD support in children may help better the understanding of VAD therapy in children. The aim of this study was to evaluate the cardiac function in children supported with HVAD, HM2 and HM3 devices by utilising computational modelling.

2. Materials and Methods

Computer simulations were performed using a cardiovascular system model which includes heart chambers, heart valves, aorta, systemic arterioles and veins, pulmonary arteries, arterioles and veins. LVAD support was simulated by implementing numerical models which simulate pressure head and flow rate (H–Q) relations in HVAD, HM2 and HM3 devices.

The cardiovascular system model simulates pressure, volume and diameter in the heart chambers; flow rate through the heart valves; and pressure and flow rate in the systemic and pulmonary circulations. In this model, left-ventricular pressure (p_{lv}) is described using the active and passive contraction components ($p_{lv,a}$, $p_{lv,p}$). Ventricular active-pressure component ($p_{lv,a}$) is described using the systolic ventricular elastance ($E_{es,lv}$), ventricular and zero-pressure volume (V_{lv} , $V_{lv,0}$) and the activation function ($f_{act,lv}$). Ventricular passive-pressure component ($p_{lv,p}$) is modelled using an exponential relationship, including volume (V_{lv}) and additional parameters (A , B).

$$p_{lv} = p_{lv,a} + p_{lv,p} \quad (1)$$

$$p_{lv,a} = E_{es,lv}(V_{lv} - V_{lv,0})f_{act,lv}(t) \quad (2)$$

$$p_{lv,p} = A \left[e^{(BV_{lv})} - 1 \right] \quad (3)$$

Left-ventricular volume (V_{lv}) is described using the left-ventricular radius (r_{lv}), long axis length (l_{lv}) and an additional coefficient (K_{lv}), which includes effects of the contraction in the long axis and scales the proportion between the left-ventricular radius and volume over a cardiac cycle. Change in the left-ventricular radius (r_{lv}) is described utilising the flow rates through the aortic and mitral valves (Q_{av} , Q_{mv}), left-ventricular volume, long axis length (l_{lv}) and the coefficient K_{lv} .

$$V_{lv} = \frac{2}{3} \pi K_{lv} r_{lv}^2 l_{lv} \quad (4)$$

$$\frac{dr_{lv}}{dt} = \frac{3(Q_{mv} - Q_{av})}{4\pi K_{lv} l_{lv}} \left(\frac{3V_{lv}}{2\pi K_{lv} l_{lv}} \right)^{-1/2} \quad (5)$$

Right and left ventricles are modelled in the same way using different parameter values. The left atrial pressure (p_{la}) and volume (V_{la}) relationship is described using elastance (E_{la}).

$$p_{la} = E_{la}(t)(V_{la} - V_{la,0}) \quad (6)$$

Left atrial volume (V_{la}) is described using the left atrial radius (r_{la}), long axis length (l_{la}) and an additional coefficient (K_{la}). Change in the left atrial radius (r_{la}) is described utilising the flow rates through the mitral valve and pulmonary vein (Q_{mv} , Q_{vp}), left atrial volume, long axis length (l_{la}) and the coefficient K_{la} .

$$V_{la} = \frac{2}{3}\pi K_{la} r_{la}^2 l_{la} \quad (7)$$

$$\frac{dr_{la}}{dt} = \frac{3(Q_{vp} - Q_{mv})}{4\pi K_{la} l_{la}} \left(\frac{3V_{la}}{2\pi K_{la} l_{la}} \right)^{-1/2} \quad (8)$$

Right and left atria are modelled in the same way using different parameter values. Heart valves are modelled as ideal diodes using pressure across a valve and the characteristic resistance. Flow rate through the mitral valve (Q_{mv}) is given below.

$$Q_{mv} = \begin{cases} \frac{p_{la} - p_{lv}}{R_{mv}} & p_{la} > p_{lv} \\ 0 & p_{la} < p_{lv} \end{cases} \quad (9)$$

The other heart valves are modelled in a similar way using different parameter values. The circulatory system includes aorta, systemic arterioles, systemic veins, pulmonary artery, pulmonary arterioles and pulmonary veins. Blood flow in the circulatory-system model is described using a lumped-parameter model, which includes electrical analogues for resistance (R), compliance (C) and inertia (L). The aortic blood pressure (p_{ao}) and flow rate signals (Q_{ao}) are given below.

$$\frac{dp_{ao}}{dt} = \frac{Q_{av} - Q_{ao}}{C_{ao}} \quad (10)$$

$$\frac{dQ_{ao}}{dt} = \frac{p_{ao} - p_{as} - R_{ao}Q_{ao}}{L_{ao}} \quad (11)$$

Here, Q_{av} and p_{as} represent aortic valve flow rate and systemic arteriolar pressure; C_{ao} , R_{ao} and L_{ao} represent compliance, resistance and inertance in the aorta, respectively. The other compartments in the circulatory system are modelled in the same way using different parameter values. The cardiovascular system model utilised in this study simulates cardiac function for children around 8–12 years of age [15]. Body surface area changes between 0.75 m² and 1.3 m² around 8–12 years of age [16,17]. Therefore, the body surface area was assumed to be 1.3 m² in a 12-year-old child in this study. Detailed information about the cardiovascular system model can be found in [15].

DCM was simulated by modifying the values of the maximal left-ventricular elastance (E_{max}) (coefficient A in the left ventricle model), left-ventricular zero-pressure volume ($V_{lv,0}$) (coefficient K in the left ventricle model) and systemic arteriolar resistance (R_{as}) in the cardiovascular system model. R_{as} was set to a healthy value during continuous-flow VAD support as the arterial pressure increased due to heart pump support, and autoregulatory mechanisms regulating the systemic arteriolar resistance accordingly. The parameter values used in the cardiovascular system model simulating healthy and DCM conditions as well as continuous-flow VAD support are presented in Table 1.

Table 1. Parameter values used in the cardiovascular system models. ^a Numbers in the brackets were used to simulate DCM and continuous-flow VAD support; ^b R_{AS} value used in the cardiovascular system models simulating the healthy condition and continuous-flow VAD support. (LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle; MV, mitral valve; AV, aortic valve; TV, tricuspid valve; PV, pulmonary valve; Ao, aorta; AS, systemic arterioles; VS, systemic veins; Po, pulmonary artery; AP, pulmonary arterioles; VP, pulmonary veins; E_{max} , maximal elastance; E_{min} , minimal elastance; A, a parameter used in the ventricle models; B, a parameter used in the ventricle models; V_0 , zero-pressure volume; l, long axis length; K, scaling coefficient used in the heart chamber models; R, resistance; L, inertance; C, compliance.).

	E_{max} [mmHg/mL]	E_{min} [mmHg/mL]	A [mmHg]	B [1/mL]	V_0 [mL]	l [cm]	K	R [mmHg s/mL]	L [mmHg s ² /mL]	C [mL/mmHg]
LA	0.4	0.2	-	-	3	4.5	2.5	-	-	-
LV	3.5 (1.3 ^a)	-	1 (0.85 ^a)	0.02	10 (17 ^a)	7	1.5 (1.4 ^a)	-	-	-
RA	0.4	0.2	-	-	3	4.5	2.5	-	-	-
RV	1.4	-	1	0.02	25	7	3.25	-	-	-
MV	-	-	-	-	-	-	-	0.002	-	-
AV	-	-	-	-	-	-	-	0.002	-	-
TV	-	-	-	-	-	-	-	0.001	-	-
PV	-	-	-	-	-	-	-	0.001	-	-
Ao	-	-	-	-	-	-	-	0.05	1E-5	0.13
AS	-	-	-	-	-	-	-	0.95 ^b (1.4 ^a)	1E-5	1.13
VS	-	-	-	-	-	-	-	0.05	-	19.35
Po	-	-	-	-	-	-	-	0.01	1E-5	3.33
AP	-	-	-	-	-	-	-	0.15	1E-5	0.13
VP	-	-	-	-	-	-	-	0.05	-	19.35

Continuous-flow VAD support was simulated using a model which describes continuous-flow VAD flow rate and the pressure head [18] as given below.

$$H_{CF-LVAD} = k n_{CF-LVAD}^2 - R_{CF-LVAD} Q_{CF-LVAD} - L_{CF-LVAD} \frac{dQ_{CF-LVAD}}{dt} + H_{rec} \quad (12)$$

$$R_{CF-LVAD} = R_1 n_{CF-LVAD} + R_2 Q_{CF-LVAD} \quad (13)$$

Here, $H_{CF-LVAD}$ and $Q_{CF-LVAD}$ represent the pressure head and flow rate, R_1 and R_2 are resistances related to friction and incidence losses, $n_{CF-LVAD}$ is the continuous-flow VAD operating speed, k is the blood flow source term, and $L_{CF-LVAD}$ and H_{rec} are the inertance and part-load recirculation in the pump. Heartware VAD, HM2 and HM3 devices were simulated using the same equation with different parameter values as given in [18]. A detailed description of the continuous-flow VAD model can be found in [18]. Continuous-flow VAD support was simulated by modifying (8) and (10) as given below.

$$\frac{dr_{lv}}{dt} = \frac{3(Q_{mv} - Q_{av} - Q_{CF-LVAD})}{4\pi K_{lv} l_{lv}} \left(\frac{3V_{lv}}{2\pi K_{lv} l_{lv}} \right)^{-1/2} \quad (14)$$

$$\frac{dp_{ao}}{dt} = \frac{Q_{av} + Q_{CF-LVAD} - Q_{ao}}{C_{ao}} \quad (15)$$

The electrical analogue of the heart chambers, and the circulatory system used to simulate the cardiovascular system and continuous-flow VAD support, has been provided in Figure 1.

Figure 1. Electrical analogue of the cardiovascular system model. R, resistance; L, inertance; C, compliance; p, pressure; MV, mitral valve; AV, aortic valve; TV, tricuspid valve; PV, pulmonary valve; la, left atrium; lv, left ventricle; ra, right atrium; rv, right ventricle; ao, aorta; as, systemic arterioles; vs, systemic veins; po, pulmonary artery; ap, pulmonary arterioles; vp, pulmonary veins.

Operating speed of the continuous-flow VADs was adjusted to simulate the same cardiac output as in the healthy cardiovascular system model and with consideration of the operating range and clinical data. Operating speeds between 2120 rpm and 2600 rpm have been reported for the Heartware HVAD device in children [19,20]. In this study, the operating speed of Heartware HVAD was set to 2600 rpm. Reported average HM2 device operating speed in patients with body surface area $<1.5 \text{ m}^2$ was $8524 \pm 4166 \text{ rpm}$ [21]. In this study, the operating speed of HM2 was set to 8700 rpm. Operating speeds around 5000 rpm and 5200 rpm have been reported for HM3 device in children diagnosed with DCM [22,23]. In this study, the operating speed of HM3 was set to 5200 rpm. Lavare cycle in Heartware HVAD was set by decreasing the pump operating speed by 200 rpm for 2 s and increasing by 400 rpm in the following 1 s over each 60 s cycle [24]. Artificial pulse in the HM3 device was simulated by decreasing the pump speed by 2000 rpm for 0.15 s, then

increasing it by 4000 rpm for 0.20 s, before operating HM3 at the set speed over each 2 s cycle [25].

The heart rate was kept at 80 bpm in all the simulations. The simulations were performed using MATLAB Simulink R2017a. The set of equations was solved using the ode15s solver. The maximum step size was 10^{-3} s and the relative tolerance was set to 10^{-3} .

3. Results

First, the simulations were performed for the healthy and DCM conditions. The ventricular pressures, aortic pressure, pulmonary arterial pressure, ventricular volumes and ventricular diameters for the healthy (Figure 2a–d) and DCM (Figure 2e–h) cardiovascular system models are presented in Figure 2.

Figure 2. (a) Left-ventricular and aortic pressures, (b) right-ventricular and pulmonary arterial pressures, (c) left and right-ventricular volumes, (d) left and right-ventricular diameters in the healthy cardiovascular system model, (e) left-ventricular and aortic pressures, (f) right-ventricular and pulmonary arterial pressures, (g) left and right-ventricular volumes, (h) left and right-ventricular diameters in the DCM cardiovascular system model. p, pressure; V, volume; D, diameter; lv, left ventricle; ao, aorta; rv, right ventricle, po, pulmonary artery.

Left-ventricular and aortic peak pressures reduced slightly in the DCM cardiovascular system model. Right-ventricular and pulmonary arterial pressures were similar in the healthy and DCM cardiovascular system models. Right-ventricular volume was slightly higher in the DCM cardiovascular model than the left-ventricular volume in the healthy cardiovascular system model, whereas left-ventricular volume as well as left-ventricular diameter increased remarkably in the DCM cardiovascular system model. Aortic pressure, left-ventricular volume and diameter under HVAD, HM2 and HM3 support are shown in Figure 3.

The amplitude of the aortic pressure signal was relatively high under HM2 support. HM3 support reduced the amplitude of the aortic pressure signal remarkably. Left-ventricular end-diastolic volume was the same under HVAD and HM2 support, whereas it was slightly lower under the support of the HM3 device. On the other hand, end-systolic volume was similar under HVAD and HM3 support and it was relatively low under HM2 support. HVAD and HM2 support resulted in similar end-diastolic left-ventricular diameters, whereas the end-systolic left-ventricular diameter was relatively low under HM2

support. The aortic pressure and left-ventricular volume and diameter under HVAD and HM3 support during the Lavare cycle and artificial pulse are shown in Figure 4.

Figure 3. (a) Aortic pressure, (b) left-ventricular volume, (c) left-ventricular diameter under HVAD, HM2 and HM3 support.

Figure 4. (a) Aortic pressure, (b) left-ventricular volume, (c) left-ventricular diameter under HVAD, and HM3 support during Lavare cycle and artificial pulse.

The HVAD Lavare cycle increased the peak pressure in the aorta, whereas HM3 artificial pulse resulted in reduced diastolic aortic pressure. HVAD increased the left-ventricular end-diastolic volume and diameter. HM3 artificial pulse also increased the left-ventricular end-diastolic volume and diameter. Left-ventricular pressure–volume loops in the healthy and DCM cardiovascular system models, under HVAD, HM2 and HM3 support and during the HVAD Lavare cycle and HM3 artificial pulse, are presented in Figure 5.

The left-ventricular pressure–volume loop shifted to the right in the DCM cardiovascular system model (Figure 5a). The size of the left-ventricular pressure–volume loop reduced under HVAD, HM2 and HM3 support. The left-ventricular pressure–volume loop also shifted to the left under heart-pump support, whereas the size of the left-ventricular pressure–volume loops was similar during HVAD, HM2 and HM3 assistance. The Lavare cycle in HVAD and artificial pulse in HM3 increased the left-ventricular pressure–volume loop area whilst shifting it to the right. The following are presented in Table 2: mean arterial pressure; pulse pressure in aorta; cardiac and mean outputs, end-diastolic and end-systolic left-ventricular volumes and diameters in the healthy and DCM cardiovascular system models, under HVAD, HM2 and HM3 support and during the HVAD Lavare cycle and HM3 artificial pulse.

Figure 5. (a) Left-ventricular pressure–volume loops in the healthy and DCM cardiovascular system models, (b) left-ventricular pressure–volume loops under HVAD, HM2 and HM3 support, (c) left-ventricular pressure–volume loops under HVAD and HM3 support during the Lavare cycle and artificial pulse.

Table 2. Haemodynamic variables in the healthy and DCM cardiovascular system models and under HVAD, HM2 and HM3 support. MAP, mean arterial pressure; PP, pulse pressure in aorta; CO, cardiac output; MPO: mean pump output; EDV, end-diastolic volume; ESV, end-systolic volume; EDD, end-diastolic diameter; ESD, end-systolic diameter. * indicates maximal values for PP, EDV and EDD whilst indicating minimal values for ESV and ESD.

	MAP [mmHg]	PP [mmHg]	CO/MPO [L/min]	EDV [mL]	ESV [mL]	EDD [cm]	ESD [cm]
Healthy CVS	82	43	4.41	92	37	4.1	2.6
DCM CVS	80	31	3.06	125	86	4.9	4.1
HVAD	81	11	4.38	91	56	4.2	3.3
HVAD Lavare	81	15 *	4.37	100 *	53 *	4.4 *	3.2 *
HM2	82	14	4.40	92	54	4.2	3.2
HM3	82	6	4.42	89	58	4.2	3.4
HM3 Artificial Pulse	81	20 *	4.38	98 *	56 *	4.4 *	3.3 *

The mean arterial pressures were similar in the healthy and DCM cardiovascular system models and under HVAD, HM2 and HM3 support. This was because systemic arteriolar resistance was adjusted in the healthy, DCM and heart-pump-supported cardiovascular system models, in consideration of the physiological systemic arteriolar resistance regulation mechanism. The aortic pulse pressure was 43 mmHg in the healthy cardiovascular system model; however, it decreased to 31 mmHg in the DCM model. Aortic pulse pressure decreased further under heart-pump support, whereas it reduced to 6 mmHg under HM3 support. However, HM3 artificial pulse increased aortic pulse pressure to 20 mmHg. The HVAD Lavare cycle also increased aortic pulse pressure by 4 mmHg. Both the HVAD Lavare cycle and HM3 artificial pulse increased left-ventricular end-diastolic volume and diameter. All the devices generated mean pump outputs which were similar to the cardiac output in the healthy cardiovascular system model. Presented in Figure 6 are the static and dynamic continuous-flow VAD pressure head—flow rate curves for the HVAD, HM2 and HM3 devices, at operating speeds of 2600 rpm, 8700 rpm and 5200 rpm, respectively.

The steep static H–Q curve at 5200 rpm for the HM3 device resulted in a relatively small dynamic H–Q loop. On the other hand, the flat H–Q curve at 8700 rpm for the HM2 device resulted in a relatively large dynamic H–Q loop. The static H–Q curve of the HVAD device at 2600 rpm remained between the H–Q curves of the HM2 and HM3 devices, resulting in an H–Q loop larger than that of the HM3 device but smaller than that of the HM2 device.

Figure 6. Static (st) and dynamic (dy) pressure head and flow rate relations of HVAD, HM2 and HM3 devices at 2600 rpm, 8700 rpm and 5200 rpm operating speeds, respectively.

4. Discussion

In this study, the cardiac function of a child's cardiovascular system under continuous-flow VAD support and the haemodynamic performance of HVAD, HM2 and HM3 heart pumps have been evaluated. All the devices generated similar pump outputs and mean aortic pressures for the selected operating speeds. The left-ventricular end-diastolic volumes and diameters were also similar under the support of HVAD, HM2 and HM3. The most remarkable difference was in the aortic pulse pressure under the support of each device. Aortic pulse pressure was relatively low under the support of the HM3 device, which has the steepest pump H–Q curve among the simulated continuous-flow VADs [18]. Steep pump H–Q characteristics result in reduced arterial pulsatility during continuous-flow VAD support [26,27]. One of the effects of reduced pulsatility in the patients with continuous-flow VADs is endothelial dysfunction [28], which may cause further adverse events in patients [29]. Therefore, continuous-flow VADs with flat H–Q characteristics that provide better pulsatility may additionally be more beneficial in improving the endothelial function in paediatric patients. It should be noted that although the constant operating speed of HM3 reduced the arterial pulse pressure, the artificial-pulse operating mode increased it remarkably. Therefore, varying-speed operating modes, such as in HM3, may help to overcome issues related to reduced pulsatility. The HVAD Lavare cycle also increased the arterial pulse pressure; however, the increased pulse pressure was somewhat similar to the arterial pulse pressure in the cardiovascular system model with HM2. Moreover, HM3's artificial-pulse mode is repeated every 2 s whilst the HVAD Lavare cycle lasts only 3 s in a 60 s period. Therefore, the HM3 artificial pulse may be more beneficial to children in comparison with the HVAD Lavare cycle.

Thrombosis rates are reportedly lower with this device when compared to its predecessor HM2 [30]. Thrombus formation on the rotating component is caused by heat generated in the pump [31]. Centrifugal pumps can generate flow rates similar to those of axial pumps, at lower operating speeds, which also generate less heat in the device. Therefore, these third-generation devices also have their advantages, such as lower complication rates in patients with continuous-flow VADs. Moreover, the HM2 device was suitable for the patients above 1.3 m² body surface area [7]. HM3 can be implanted to patients with a body surface area lower than 0.8 m², as reported in [9], and HVAD was suitable for the patients above 0.6 m² body surface area [10]. Again, patients with a relatively small body surface area can be implanted with HM3 or HVAD.

Left-ventricular end-diastolic diameter may be one of the predictors of myocardial recovery in children. A smaller left-ventricular end-diastolic diameter during VAD support may result in myocardial recovery, whereas insufficient change in left-ventricular end-diastolic diameter may be a predictor of mortality under VAD support [32]. HM3 achieved slightly better unloading at the end of diastole in comparison to HVAD and HM2. The mechanism of myocardial recovery under VAD support remains unclear and may depend on different factors. However, the simulation results show that HM3 can achieve better end-diastolic unloading for the same pump output and mean arterial pressure.

Baroreflex regulation of systemic arteriolar resistance was adjusted manually in this study. It was assumed that systemic arteriolar resistance in the cardiovascular system model was maintained at the healthy levels with the restored mean arterial pressure under continuous-flow VAD support. Any changes in arterial blood pressure are detected by baroreceptors in the walls of the large systemic arteries and are then transmitted to the central nervous system. A drop in arterial blood pressure stimulates the sympathetic nervous system. The response of the cardiovascular system to a pressure drop in the large arteries is to increase the systemic peripheral resistance by constricting the arterioles [33]. This mechanism has been modelled [34] and utilised to evaluate continuous-flow VAD support in adults [35]. In this study, it was assumed that the baroreflex regulation responds in a similar way to the continuous-flow VAD support in paediatric patients.

It should be noted that HM2 was replaced by HM3 [7] and HVAD was recalled due to technical issues [36]. Therefore, HM3 remains the most viable alternative to pulsatile Berlin EXCOR VAD in children requiring mechanical circulatory support.

Lumped-parameter models, as in this study, have been used to evaluate the choice of the VAD that could be implanted to improve the hemodynamic benefits. Moreover, models could allow the simulation of rare physiological conditions and their possible solutions [37]. A direct comparison of three different continuous-flow VADs with different pressure–flow rate characteristics can help to evaluate haemodynamic outcomes in children, and therefore can provide insights into the selection of more suitable devices for paediatric patients.

5. Conclusions

In this study, continuous-flow left-ventricular assist devices, which are proposed as alternatives to pulsatile Berlin EXCOR VAD, were evaluated using numerical simulations. The main difference in the results was aortic pulse pressure which can affect endothelial function in arteries and further associated complications. The HM3 constant-speed support mode reduced aortic pulse to 6 mmHg whilst the artificial-pulse operating mode increased aortic pulse pressure to 20 mmHg. HM3 may also be more beneficial in reducing complication rates associated with altered arterial pulsatility. Although only HM3 remains an option for children among the simulated devices, the findings in this study may also help to improve pump-support modes in children.

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