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Computational analysis of the importance of flow synchrony for cardiac ventricular assist devices

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Abstract

This paper presents a patient customised fluid–solid mechanics model of the left ventricle (LV) supported by a left ventricular assist device (LVAD). Six simulations were conducted across a range of LVAD flow protocols (constant flow, sinusoidal in-sync and sinusoidal counter-sync with respect to the cardiac cycle) at two different LVAD flow rates selected so that the aortic valve would either open (60 mL s^{-1}) or remain shut (80 mL s^{-1}). The simulation results indicate that varying LVAD flow in-sync with the cardiac cycle improves both myocardial unloading and the residence times of blood in the left ventricle. In the simulations, increasing LVAD flow during myocardial contraction and decreasing it during diastole improved the mixing of blood in the LV cavity. Additionally, this flow protocol had the effect of partly homogenising work across the myocardium when the aortic valve did not open, reducing myocardial stress and thereby improving unloading.

Keywords

Fluid–structure; Computational model; Cardiovascular; Tissue mechanics

1 Introduction

Heart failure is the leading cause of hospitalisation among older adults in Western society with a lifetime risk of 20% at age 40. Despite improved medical and surgical techniques, mortality after the onset of heart failure remains high, ranging from 20 to 50% [6]. Orthotropic heart transplantation is recognised as the best therapy for end-stage heart failure [26]. However, approximately 20 to 30% of potential recipients die while waiting for a donor heart [29]. Due to this shortage, left ventricular assist devices (LVADs) are often used as a bridge to transplant [1].

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Conflict of interest statement

None declared.

The role of these LVAD pumps is to reduce the mechanical load on the heart by pumping blood from the left ventricular (LV) apex directly to the aorta, with the implantation of these devices significantly reducing both LV pressure and volume [9]. Post implantation, it is standard practice for clinicians to tune LVAD flow so that the aortic valve opens occasionally to prevent it fusing shut [27]. However, the impact of valve opening on myocardial unloading and the residence times of blood within the ventricle remains unknown. Both these factors are of critical importance with respect to improving treatment outcome for patients – too much unloading can lead to myocardial atrophy, while too little results in the myocardium remaining over-stressed [14]. A further consideration is the impact of LVAD flow on blood residence times, where inadequate recirculation has the potential to increase the risk of thrombosis formation [2]. Tuning the device to optimise for these factors involves varying both LVAD flow rate and LVAD flow synchrony – i.e. whether the LVAD cannula outflow is constant or varies through the cardiac cycle. However, these parameters result in substantial variation in cardiac behaviour, ranging from determining whether the aortic valve opens at all, through to the extent to which LV volume changes through the cardiac cycle.

A central difficulty for this type of optimisation is the challenge of observing cardiac function and cardiovascular flows under LVAD support using standard medical image modalities, such as MRI and echocardiography, due to the positioning of the pump, along with its metallic components. This context motivates the application of mathematical modelling techniques as an investigative tool for studying the behaviour of the ventricle under LVAD support and analysing its efficacy as a pump. For such analyses to facilitate the optimisation of LVAD support, the interaction at the core of ventricular function needs to be addressed – i.e. the coupling between blood flow in the ventricular chamber and the myocardium. As a result, coupled fluid–solid mechanical models are required with the ability to support investigations into the impact of LVAD support on ventricular hemodynamics and myocardial mechanics.

Several coupled fluid–solid mechanical LV models currently exist in the literature, ranging from the pioneering work of McQueen and Peskin [17,25] through to recent models incorporating greater degrees of physical realism, in particular, in the description of myocardial behaviour [22]. These models have been used to investigate blood flow within the ventricular cavities and the efficiency of the heart as a pump from diastole [3] through to systole [11,22,32,33]. Recently, we [15,16] have extended a non-conforming finite element fluid–solid mechanics scheme [21] to facilitate the simulation of LVAD supported LVs through the full cardiac cycle. Using a fictitious domain (FD) [31] method to prescribe the LVAD cannula, the application of this approach enables the interaction between the cannula and the myocardial wall to be captured, facilitating the simulation of the full range of cardiac behaviour.

In this study we apply this framework for the first time to a patient customised geometry to present the first (to our knowledge) numerical investigation into the impact of aortic valve opening and LVAD flow synchrony on ventricular hemodynamics and myocardial mechanics. Specifically, the developed model is applied to investigate the mixing of blood

within the LV chamber, as well as the efficiency of myocardial work transduction under different LVAD flow protocols.

2 Materials and methods

2.1 Model framework

Derived from the principles of conservation of mass and momentum, and as outlined in detail in our previous publications [16,22], we have developed a model that provides a physiological description of the myocardium and ventricular blood flow. In brief, the model was solved using a non-conforming Galerkin finite element scheme to enable varying degrees of refinement to adequately resolve the blood and myocardial spatial domains. This scheme enables high levels of physiological detail (including the complex fibre architecture [13] and biophysically based constitutive laws) to be incorporated.

To resolve the physical system, ventricular blood flow and myocardial mechanics were modelled using the arbitrary Lagrange–Eulerian form of the Navier–Stokes equations [20] and the quasi-static finite elasticity equations [23], respectively. To enforce continuity between the solid myocardial wall and the fluid ventricular chamber, velocities were equated over their common interface [21]. This constraint was applied by introducing a Lagrange multiplier to enforce equal, but opposite, tractions across the endocardial boundary. To incorporate the LVAD cannula into the model, a zero velocity boundary condition was implemented on the cannula wall using the fictitious domain method whereby a second Lagrange multiplier was applied to the FEM weakform. This method enables the cannula boundary to move through the fluid domain, resolving the numerical issues resulting from the deformation of the fluid mesh [15]. Additionally, it has been demonstrated that application of the fictitious domain terms yields adherence to the velocity constraint weakly [30,31], and the method is applied to many cardiovascular applications. Furthermore, the combination of the two Lagrange multipliers implicitly resolves the contact problem of an immersed rigid body in a deformable chamber. As a result the model system is capable of resolving the complete range of cardiac motion – including contact between the myocardium and the LVAD cannula [15].

Solving the fluid–solid mechanical model through a whole cycle requires the addition of accurate systemic constraints on the flow model. This was achieved by integrating the 3D FSI model with a 0D Windkessel representation of systemic circulation. In this work, we coupled the Shi and Korakianitis 0D Windkessel model [28] using a fixed point prescribed flow rate technique [16]. Using this technique, flow was prescribed according to the pressure gradient across the valve using Bernoulli's equation for the conservation of energy along the same streamline. Valve opening was prescribed to occur when LV lumen pressure exceeds aortic sinus pressure. To approximate opening and closing in the 3D model, the valves were defined as functions on the mitral and aortic boundaries, with the radius of the open valve assumed to be proportional to flow rate. The proportionality constant was fitted to match observed human data, ≈ 46 ms and ≈ 24 ms for the mitral [34] and aortic [24] valves respectively, see Appendix A for details.

To capture the mechanical properties of the myocardium, the finite elasticity stress tensor was defined as a combination of passive and active components. The stress further incorporated information about myocardial structure, by the introduction of an orthonormal fiber tensor, to denote the fibre, sheet and normal directions of the tissue [7,19]. In this paper, the passive constitutive law was defined using a modified form of the Costa constitutive law [4] based on the strain energy functions W and W_{iso} , where W represents the Costa constitutive contribution and an isotropic stiffness component (see [22] for details of the incorporation of this component). Additionally, to approximate the interaction between the cannula base and the myocardium, the myocardial wall was assumed to be stiffer at the junction between the LVAD cannula base and the myocardial wall. Active contraction in the tissue was generated using the Niederer contraction model [18] chosen due to the limited number of parameters enabling a more unique fit to patient data [18]. This 6 parameter model captures the length dependent rates of tension development, along with peak tension.

2.2 Patient model

This framework was applied to a patient specific LV geometry which was constructed based on 422 short axis CT image slices taken at end diastole from a 53 year old heart failure patient with an implanted LVAD, all data was acquired as part of a local ethics committee at the German Heart Centre approved protocol consistent with the principles expressed in the Declaration of Helsinki and informed consent was obtained from the patient. The spatial resolution of the image stack was $0.4 \text{ mm} \times 0.4 \text{ mm}$, in the CT image plane, and 0.6 mm in the through plane direction. Digitisation of the image data was performed by Phillips Research and the resulting binary segmentation was used to construct the geometric myocardial mesh. Fig. 1 highlights each stage of the mesh generation procedure. A cubic Lagrange myocardial mesh was constructed from an ellipsoidal template using an automated meshing tool that implements the procedure previously outlined [12]. Mean error from the fitting procedure (with respect to the normal distance between binary data and the fitted mesh) was $0.72 \pm 1.05 \text{ mm}$. The final fitted cubic Lagrange mesh was interpolated from the warped cubic Hermite geometry. The resulting cubic hexahedral mesh consisted of 324 elements, with a through wall thickness of 3 elements. An idealised fibre geometry, $\pm 60^\circ$ with respect to the endo/epicardial surfaces, was defined within the myocardial geometry.

Within the ventricular cavity a linear tetrahedral fluid mesh, consisting of $\approx 3.2 \times 10^4$ elements, was constructed using the software package CUBIT,¹ with a characteristic mesh length of 3.2 mm . The linear mesh was modified to provide a curvilinear description (quadratic Crouzeix–Raviart [5] elements) of the cavity by projecting surface nodes onto the endocardial surface. Internal nodes were unchanged maintaining the linear spatial description of non-boundary fluid elements. The LVAD cannula introduced by the fictitious domain approach was incorporated using the geometry provided by Berlin Heart. The boundary mesh was constructed, with a characteristic length equivalent to that of the fluid mesh, from 544 linear triangular elements.

¹<http://cubit.sandia.gov>.

2.2.1 Experimental protocol—Simulations on the patient model were performed using a variety of LVAD flow protocols, ranging from constant LVAD flow rates at 60 and 80 mL s⁻¹, to flow varying sinusoidally – though always positive – through the cardiac cycle (either increasing or decreasing during systole) with mean flow rates of 60 and 80 mL s⁻¹. The protocols, defined in Table 1, were selected to test the impact of both aortic valve opening² (with a mean flow rate of 60 mL s⁻¹ the valve opened while at 80 mL s⁻¹ it remained shut) and whether increasing or decreasing LVAD outflow during systole impacted myocardial unloading or the residence times of blood within the ventricular chamber.

For each flow protocol, simulations were performed for two heart beats, each of one second, consisting of 2500 time steps per beat, with a time step of 0.00025 s during the contractile phases and 0.001 s during diastole. A linear activation sequence, endocardium to epicardium, was defined with a period of 0.05 s. The resulting simulations, initiated from end diastole, consisted of $\approx 5.5 \times 10^5$ fluid and $\approx 3.4 \times 10^4$ solid degrees of freedom. The same external model parameters (i.e. Windkessel and contraction models) were used in all cases. All simulations converged on repeating pressure volume loops, see Fig. 3.

2.2.2 Passive and active myocardial parameter fitting—To incorporate the residual strain, present in the myocardium at end diastole, a zero-stress, or reference state of the myocardium was estimated using the methods previously outlined [15,22]. Here, the Costa constitutive parameters were fitted to the Klotz pressure volume relationship [10] defined by the end diastolic volume of 240.95 mL and pressure of 13.13 mmHg. Since patient specific pressure data was not available, the pressure value was taken from equivalent LVAD supported patient data [9]. The contraction parameters were tuned so that LV stroke volume was ≈ 50 mL and peak systolic pressure was between 100 and 120 mmHg when the LVAD was switched off. This was consistent with observations [9]. Additionally, due to the slow rate of myocardial relaxation typically observed in cardiomyopic heart failure patients [8], the desired durations of isovolumetric contraction and relaxation were 0.1 s and 0.2 s, with a systolic period of 0.2 s.

The pressure volume relationships from the iterative updates of the passive fitting procedure (along with the ideal Klotz relationship) are shown in Fig. 2, along with a sampling of PV relationships from a set of simulations solving only the solid problem across a range of parameters. The final fitted parameters are provided in Tables 2 and 3.

2.2.3 Initial and boundary conditions—Solid only simulations were performed to converge the myocardial and Windkessel models on repeating pressure volume loops for each of the flow protocols. The solutions from each of these simulations were used as the initial conditions for their respective fluid–solid coupled simulations. Due to differences in afterload in the 60 and 80 ml s⁻¹ cases, initial end-diastolic volumes were 5–10% lower in the 80 ml cases. The relevant LV and Windkessel model initial conditions are provided in Table 4. Note that due to continuous flow through the LVAD, increased LVAD flow rates led to increased aortic pressures.

²Model valves were defined as functions on the mitral and aortic fluid boundaries, Γ_{mi} and Γ_{ao} . Full description of these functions are provided in [15,22].

3 Results

In both the L_{60} and L_{80} cases, increasing LVAD outflow during systole and reducing it during diastole increased the range of LV volumes through the cardiac cycle and reduced peak LV pressure. The opposite effect was observed when LVAD outflow decreased during systole. Comparing the L_{60} and L_{80} cases, LV volume was significantly lower in the L_{80} cases, while peak LV pressures were lower in all equivalent L_{80} simulations (see Fig. 3). Additionally, the range in LV volume was greatest in the L_{80+} case and smallest in the L_{80-} case.

It is thus convenient, particularly given that systole does not necessarily occur in supported hearts at high LVAD flow rates, to consider two broad periods of cardiac behaviour, the contractile phases (i.e. IVC, systole and IVR) and diastole. Using this distinction to divide the results, the blood flow streamlines and myocardial displacements from selected time points during the second heart beat in the L_{60} cases are shown in Fig. 4, while the endocardial fluid pressures at the same time points are presented in Fig. 5. With the exception of the 0.21 s time point where the aortic outflow was not observed, the flow profiles in the L_{80} cases were similar to those observed in Fig. 4.

At the opening of the aortic valve (0.21 s), significant flow in the direction of the valve was produced, however, due to the weakness of aortic flow as a result of continued LVAD outflow, sustained helical features were observed at the far wall from the valve. During IVR (0.41 s) low flow velocities were observed within the cavity, driven primarily by LVAD outflow. Diastolic inflow (0.70 s and 0.90 s) resulted in the formation of large vortices within the cavity in conjunction with peaks in mitral inflow. Comparing the various LVAD outflow profiles, when LVAD outflow was in-sync with the cardiac cycle (the L_{80+} case) stronger vortices were observed during diastole, as observed in Fig. 4.

Comparing simulated pressures, pressure waves were observed traveling through the ventricular cavity during both the contractile phases and diastole. High pressure gradients in the direction of flow were observed during both peak aortic outflow (0.21 s) and peak diastolic inflow (0.70s). Comparing the different LVAD outflow profiles, greater pressure gradients were observed in conjunction with lower LVAD outflow, helping drive the stronger vortices observed in these cases.

3.1 Ventricular resonance time

To compute ventricular resonance times³ in the LV, particles were tracked through the solution flow field, providing an analysis of the recirculation of blood within the simulated ventricular cavity. Particles were seeded at regular, 0.046 s, intervals during the first simulated diastolic period and were tracked for two cardiac beats by looping the simulation results. Similar particle motions were observed in both the L_{60} and L_{80} cases. For the L_{60} cases, a visualisation of the movements of particles within the LV cavity is provided in Fig. 6. Fig. 7 details the percentage of particles, grouped according to diastolic periods (early,

³Resonance time was defined as the time a particle, seeded at the mitral valve, remained in the ventricular chamber before ejection via either the aortic valve or the LVAD cannula.

diastasis, late), remaining in the LV cavity over time, while a summary of the composition of ejected fluid is given in Table 5.

Varying the synchrony of LVAD outflow dramatically altered the ejection pattern of particles from the cavity. Immediately obvious when examining the particle motion is the correlation between LVAD flow rate during diastole and the basal motion of particles due to vortices in the LV chamber. The greater LVAD diastolic outflow, the slower this motion. This was consistent with the weaker vortices observed during the diastolic phases in the L_{s60-} case in Fig. 4. Overall, the higher rate of circulation in the L_{s60+} case improved mixing of the fluid, visible at 1 s in Fig. 6. Further evidence for this improved mixing can be seen in the traces in Fig. 7 where the percentage of ejected particles form a more narrow grouping in the L_{s60+} case compared to either the L_{60} or L_{s60-} cases. This trend was less apparent in the L_{80} cases. However, the different rates of particle ejection between early diastole, diastasis and late diastole observed in the L_{s60-} and L_{s80-} cases highlight poorer mixing of fluid when the LVAD flow rate is out of phase with the cardiac cycle.

The general metrics reported in Table 5 provide a more quantitative basis for comparing the simulated behaviours. By associating particles with diastolic inflow volumes, an estimate of the volume ratios of aortic and LVAD outflow could be made. Given the volume and low ejection fraction of the patient LV, higher rates of ejection of older fluid (i.e. fluid that has resided in the cavity for multiple cardiac beats) are important. Surprisingly, using this metric, both the positive and negative sinusoidal cases performed strongly, in contrast to the constant LVAD flow simulations. A possible explanation is that the improved mixing in the L_{s60+} and L_{s80+} cases resulted in a more even composition of systolic outflow, while the poorer mixing in the L_{s60-} and L_{s80-} cases led to periods when the predominance of outflow was from preexisting fluid (or vice versa). Both instances would result in improved ejection rates for older particles. The poor ratios observed from the negative sinusoidal cases in the % S.V. beat 1 column in Table 5 provide evidence for this explanation. This result does not, however, rule out the possibility that while a high percentage of older fluid was ejected in the negative sinusoidal cases, this was only true in an averaged sense and certain regions may have exhibited poor recirculation due to the lower levels of mixing.

3.2 Myocardial energetics

A summary of the transduction of mechanical work at the cellular level to whole organ pump function under the different simulated LVAD flow protocols is provided in Table 6. Over the second heart beat, the total change in stored potential elastic energy was small, < 5% of the total energy present (fluid kinetic and solid potential) at the start and end points of the cardiac cycle. The discrepancies can be accounted by minor variations in the LV pressure–volume relationship between the first and second beats. As expected, increased LVAD outflow reduced the work performed by the myocardium. This was particularly evident in the cases where LVAD outflow reduced during the contractile phases. Similarly, total energy transported out of the LV decreased with LVAD flow rate. In general it was noted that in cases where flow output during the contractile phases was higher, either due to aortic valve opening or increased LVAD outflow in this phase, the greater the energy transported from the system. This was due to elevated boundary tractions caused by higher

contractile cavity pressures. Finally, the total energy lost over the cardiac cycle was dominated by advection of momentum to the system circulation, which were greatest in simulations with higher peak outflows, i.e. $L_{sX\pm+}$ cases. Greater peak outflow also increased the rate of viscous energy dissipation, further amplifying this effect.

Of particular interest with respect to determining the optimal degree of LV unloading under LVAD support is the energetics of the myocardium. While gross myocardial metrics only provide a partial picture of myocardial energetics, how work is spatially distributed, in particular between regions of positive and negative work, enables a better comparison to be made of the impact of LVAD support. To this end, a visualisation of the spatial distribution of work during the L_{60} and L_{80} cases is shown in Figs. 8 and 9.

Immediately obvious, with respect to the constant flow simulations, was the relationship between LVAD outflow and the spatial dyssynchrony of work when the aortic valve did not open (the L_{80} cases). This was particularly apparent during periods of peak tension, i.e. 0.12 s, 0.15 s and 0.21 s. In comparison, in the L_{60} cases, it was evident that during aortic ejection (0.21 s) total work was increased and distributed more homogeneously. This can be explained by the relationship between outflow and work – out-flow enables myocyte shortening as generated muscular tension is released, producing pump work. Not only did the rate of myocardial work increase during systole, but volume change was connected to cavity pressure, and by extension myocardial energetics. As a result, increases in local work no longer acted to shift fluid within the ventricular chamber and in turn redistributing stored potential energy to another region. Instead, work acted to eject more fluid from the LV cavity. Therefore, the net result of systolic ejection was to increase the spatial homogeneity of work in the myocardium. Outflow via the LVAD cannula, as it was unconnected to ventricular behaviour, did not have the same effect.

The effect of systolic outflow, with respect to different LVAD flow protocols, can be seen when comparing Figs. 8 and 9. In the L_{80} cases, where the aortic valve did not open, heterogeneity of work increased as LVAD outflow decreased – as expected since similar tensions were generated in all three cases, yet work was lower in the L_{s80-} case. However, this effect was substantially reduced in the L_{60} cases, due to the homogenising effect of systolic outflow.

4 Discussion

The results presented in this paper provide a detailed analysis of model performance under different LVAD flow regimes on a patient LV geometry. Significant variations in hemodynamic and myocardial dynamics were observed across a range of loading conditions investigated and these results provide an insight into how LVAD support impacts gross LV function. This section discusses the conclusions that can be drawn from these simulations, taking into account the impact of model limitations on these conclusions.

4.1 Particle tracking

A significant observation from particle tracking results was that the rate of fluid mixing was correlated with lower LVAD outflow during diastole. A possible explanation for this result

relates to the increase in mitral inflow during diastasis in cases where LVAD outflow was higher. During diastole, incoming fluid displaces pre-existing fluid at the LV apex, forcing this volume towards the LV base. At lower diastolic LVAD flow rates, this displacement induced the formation of vortices that grew to fill the LV cavity during diastasis. These vortices play an important role in circulating fluid through the cavity. The increase in mitral inflow, particularly during diastasis when LVAD outflow was higher, acted to block vortex formation, which resulted in two layers of fluid, a basal layer of older fluid and an apical layer consisting of fluid from the current diastolic interval. Mixing between these layers was observed to be slow. This displacement of fluid can be clearly seen in the L_{s60-} case in Fig. 6.

Additionally, the importance of greater LVAD flow rates during the contractile phases can also be extrapolated from these results. If LVAD outflow decreases during this period, and limited/no outflow occurs via the aortic valve, overall flow in the ventricle will also decrease. This will have the effect of reducing mixing during this phase. This hypothesis highlights the importance of aortic outflow in the mixing of blood in the ventricle. Furthermore, since increasing LVAD outflow during the contractile phases acts as a pseudo-systolic event, this theory can also explain why the weaker vortices observed during the contractile phases in the positive sinusoidal cases did not have observable negative impacts on particle mixing.

4.2 Myocardial energetics

The analysis of myocardial energetics demonstrates that different LVAD flow rates significantly alter the dynamics of the myocardium. With respect to the constant flow simulations, increased LVAD outflow reduced the loading on the myocardium, reducing both the amount of stored potential energy and the amount of mechanical work available for whole organ pumping during both the contractile phases and diastole. Regarding the sinusoidal flow simulations, the predominant effect was observed in myocardial work where greater outflow corresponded to greater mechanical work performed. During diastole, large variations in rates of potential energy increase were observed. However due to low cavity pressures during this phase, the significance of this effect on overall myocardial unloading is questionable.

The observed homogenising effect of systolic outflow on the spatial variation work enables an interesting hypothesis to be developed regarding the importance of aortic valve opening and the choice of LVAD flow protocol. If the aortic valve does not open, these simulations indicate that more homogeneous myocardial behaviour can be achieved by synchronising increases in LVAD outflow with the contractile phases. However, if the aortic valve does open, the importance of LVAD flow synchrony on myocardial energetics is less important and the choice of flow protocol can be weighted more towards its impact on fluid mixing in the ventricle.

4.3 Summary

The primary conclusion from the particle tracking results, that greater fluid mixing occurs when LVAD outflow is lower during diastole, fits well with the spatial variation of work

results. Given that work was more spatially homogeneous in the L_{s80+} case when the aortic valve did not open, and that improved mixing was observed in both that case and the L_{s60+} case, these results indicate that increasing LVAD outflow during systole and decreasing flow during diastole improves both the spatial distribution of work and the mixing of fluid in the ventricular chamber.

Of fundamental importance with regard to using the predictions resulting from this study in a clinical setting, is the effect of model assumptions on the observed results and predictions. One of the primary model limitations was the boundary condition used to constrain myocardial movement. In the model the ventricular basal plane was fixed, restricting the physiological realism of myocardial deformation. The impact of this on both myocardial deformation and the hemodynamics of blood within the ventricle is unknown. Additional considerations, such as the models lack of trabeculae, valves, the smoothness of the endocardial surface and the fluid inflow/outflow boundary conditions will also all have an impact on model behaviour. Finally activation of active tension at the beginning of isovolumic contraction was assumed spatially homogeneous based on the assumption that the time scale of the spread of electrical activation is significantly shorter than the features of fluid–solid interaction of interest predicted by the model.

With respect to overall simulation behaviour under different LVAD flow regimes, certain aspects, in particular peak systolic pressure and early diastolic inflow, were dependent on the contraction parameters chosen. Furthermore, the Windkessel model parameters were unchanged in each case, resulting in the simulation results being possibly an underestimate the degree of unloading due to LVAD support. This is because greater ventricular output leads to reduced preload and afterload, reducing the stress on the system. By maintaining the Windkessel parameters constant across all simulations, the extent of these changes was not fully captured by the model. Finally, due to the lack of experimental and patient data, it is not currently possible to correlate predicted results with physical observations. As a result, further studies are required. However, in spite of these model limitations, the model provides a useful platform for investigating the impact of LVAD support on ventricular hemodynamics, myocardial stress and myocardial work.

The simulation results in this paper have created hypotheses which provide avenues and directions for future research, both computational and experimental, on the impact of LVAD support on ventricular function. If validated, the predictions have the potential to significantly alter treatment protocols in patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1. Myocardial geometry fitting to patient image data. Top left, digitised binary myocardial map superimposed against a CT slice, LVAD cannula visible; top right, the fitted myocardial geometry compared with the binary myocardial map; bottom left, the fitted myocardial geometry superimposed against a CT slice; and bottom right, visualisation of the $\pm 60^\circ$ fibre geometry.

Fig. 2.

Fitting of patient passive myocardial parameters. Left, iterative updates of the passive PV relationship (iteration 1–4), fitted for an end diastolic volume and pressure of 240.95 mL and 13.13 mmHg respectively. Red shows the reference Klotz relationship; Right, a sample of PV loops from the fitting of the active tension and Windkessel models. The models were fitted for a stroke volume of $\approx 50 \text{ mL s}^{-1}$ and peak LV pressure during systole of between 100 and 120 mmHg. The final fitted relationship is in red. (For interpretation of the references to colour in this figure caption, the reader is referred to the web version of this article.)

Fig. 3.

LV pressure volume loops from the heart beat of the patient simulations. Left, the PV loops from the L_{60} cases; and right, the PV loops from the L_{80} cases. c , $+$ and $-$ refer to the continuous, in sync and counter sync LVAD flow profiles, respectively. Red, blue and black markers indicate the time points shown in Figs. 4, 5, 6, 8, and 9. Note that volumes in the L_{80} cases were 5–10% lower than in the L_{60} cases.

Fig. 4.

(a) Fluid streamlines and myocardial displacements from the second simulated heart beat of the L_{60} LVAD flow case: the results are visualised at systole (0.21 s), IVR (0.41 s) and diastole (0.70 s and 0.90 s). (b) Comparison of streamlines at 0.70 s between the L_{s60+} , L_{60} , and L_{s60-} : streamlines indicate variations in the strength of the vortices between the three cases. Note that due to LVAD outflow the isovolumetric phases were not strictly isovolumetric. (For interpretation of the references to colour in this figure caption, the reader is referred to the web version of this article.)

Fig. 5.

LV cavity pressure from the second simulated heart beat of the L_{60} LVAD flow regime cases: top row, L_{s60+} , centre row, L_{s60+} , and bottom row L_{s60-} . The results are visualised at IVC (0.12 s), systole (0.21 s), IVR (0.41 s) and diastole (0.70 s and 0.90 s). The range in pressure values (given in mmHg) was constant across each column of subfigures and is provided at the bottom of each column. (For interpretation of the references to colour in this figure caption, the reader is referred to the web version of this article.)

Fig. 6.

(a) Visualisation of seeded particles at various points in the cardiac cycle during the L_{60} case coloured by their seed time with respect to the first set of seeded points. Particles were seeded at intervals of 0.046 s with an initial seed time of 0.02 s into the first diastolic period (i.e. 0.52 s into the simulation). Two complete beats were tracked by looping over the second heart beat. Particle locations are shown at selected time points through the two tracked heart beats. Note $t=0$ is equivalent to the commencement of diastole. b) Comparison of particle mixing after 1 s between the L_{60} , $L_{60\ s+}$ and $L_{60\ s-}$ cases: Note the increased degree of mixing of particles throughout the ventricular cavity in the $L_{60\ s+}$ case. (For interpretation of the references to colour in this figure caption, the reader is referred to the web version of this article.)

Fig. 7.

The percentage of seeded particles remaining in the ventricle over time since seeding from the patient LV simulations. Results are summarised by the period of diastole within which they were seeded i.e. early diastole (E.D.) 0.0–0.18 s, diastasis (D.) 0.18–0.41 s and late diastole (L.D.) 0.41–0.50 s. Plots are shown for each simulation, top two rows the constant LVAD flow simulations and bottom two rows, the sinusoidal LVAD flow results.

Fig. 8.

Spatial distribution of work during the contractile phases from the L_{s60+} , top, L_{60} , centre, and L_{s60-} bottom simulations. The visualised results are from the second simulated heart beat in each simulation. Spheres are located at myocardial element centrepoints and are scaled by the magnitude of elemental rate of work (J s^{-1}). Sphere colour, blue to red, is the mean intensity of work ($\text{J s}^{-1} \text{m}^{-3}$) within the element. Total rates of work (J s^{-1}) for each simulation at each visualised time point (in sequential order) were $L_{60} = [1.30, 1.71, 1.61, 4.02, 0.369]$, $L_{s60+} = [1.36, 1.99, 2.01, 4.27, 0.747]$, and $L_{s60-} = [1.23, 1.43, 1.20, 3.45, 7.27 \times 10^{-2}]$. (For interpretation of the references to colour in this figure caption, the reader is referred to the web version of this article.)

Fig. 9.

Spatial distribution of work during the contractile phases from the L_{s80+} , top, L_{80} , centre, and L_{s80-} bottom simulations. The visualised results are from the second simulated heart beat in each simulation. Spheres are located at myocardial element centrepoints and are scaled by the magnitude of elemental rate of work (J s^{-1}). Sphere colour, blue to red, is the mean intensity of work ($\text{J s}^{-1} \text{m}^{-3}$) within the element. Total rates of work (J s^{-1}) for each simulation at each visualised time point (in sequential order) were $L_{80} = [1.27, 1.71, 1.74, 1.21, 0.555]$, $L_{s80+} = [1.32, 2.03, 2.24, 1.88, 1.00]$, and $L_{s80-} = [1.20, 1.40, 1.21, 0.450, 5.38 \times 10^{-3}]$. (For interpretation of the references to colour in this figure caption, the reader is referred to the web version of this article.)

Table 1

LVAD flow protocols for the patient study. Time $t=0$ was taken with respect to the start of isovolumetric contraction. In sync refers to increasing LVAD flow during systole while counter sync refers to decreasing flow. Total flow rate through one cardiac cycle in the sinusoidal LVAD protocols was the same as for their equivalent constant flow rate cases.

Simulation	Flow rate(mL s ⁻¹)	Description
L_{60}	$Q_{LVAD} = 60$	Constant flow rate
L_{80}	$Q_{LVAD} = 80$	Constant flow rate
L_{s60+}	$Q_{LVAD} = 60 + 45 \sin(2\pi t)$	Sinusoidal flow rate, in sync
L_{s60-}	$Q_{LVAD} = 60 - 45 \sin(2\pi t)$	Sinusoidal flow rate, counter sync
L_{s80+}	$Q_{LVAD} = 80 + 60 \sin(2\pi t)$	Sinusoidal flow rate, in sync
L_{s80-}	$Q_{LVAD} = 80 - 60 \sin(2\pi t)$	Sinusoidal flow rate, counter sync

Table 2

Fitted Costa law parameters for the patient myocardial model. Note α_{ij} is symmetric.

$C(\text{KPa})$	$\alpha_{1,1}$	$\alpha_{2,2}$	$\alpha_{3,3}$	$\alpha_{1,2}$	$\alpha_{1,3}$	$\alpha_{2,3}$	α_0	C_ϕ
380.05	33.41	6.45	3.61	14.68	10.92	4.83	33.41	3000

Table 3

Fitted parameters for the Niederer contraction model.

T_0 (KPa)	t_{r0}	t_d	a_1	a_2	a_3
120	0.11 s	0.199 s	2.0	0.7	3.2

Table 4

Initial LV pressures and volumes, as well as the Windkessel model initial values for the left atria (LA) and aorta (Ao). The values were taken from the solid only models at end diastole, after convergence on a repeating pressure volume loop. Pressures (P) are given in mmHg, while volumes (V) are in mL. All initial flow rates across the mitral and aortic valves, as well as the LVAD cannula, were zero.

	LV parameters		Windkessel parameters		
	V_{LV}	P_{LV}	P_{LA}	V_{LA}	P_{Ao}
L_{60}	232.37	10.60	9.79	42.49	107.49
L_{80}	225.55	8.75	8.35	36.19	120.18
L_{s60+}	234.38	11.21	10.23	44.41	101.74
L_{s60-}	230.01	9.92	9.30	40.33	113.56
L_{s80+}	227.79	9.32	8.74	37.90	114.22
L_{s80-}	222.35	7.99	7.82	33.87	126.80

Table 5

Table summarising the constitution of ejected blood from the LV cavity. S.V. is the stroke volume (defined as volume of fluid outputted by the ventricle per beat) of the LV; E.F. is the ejection fraction of the ventricle (defined as the ratio S.V. over end diastolic volume); % S.V. beat 1 is the percentage of the S.V. made up of fluid that entered the chamber during the current cardiac cycle; % S.V. beat 2 is the percentage of the S.V. made up of fluid that entered the chamber during the previous cardiac cycle; E.F. old cavity vol. (%) is the fraction of fluid that has been in the cavity greater than two heart beats exiting the LV per beat.

	S.V. (mL)	E.F. (%)	% S.V. beat 1	% S.V. beat 2	E.F. old cavity vol. (%)
L_{60}	69.69	26.64	23.41	30.72	22.99
L_{s60+}	68.22	27.38	22.24	23.63	28.78
L_{s60-}	71.39	26.10	15.74	28.88	27.74
L_{80}	80.00	30.31	27.89	26.10	28.26
L_{s80+}	80.00	32.43	32.14	22.52	31.01
L_{s80-}	80.00	28.54	20.74	24.51	31.25

Table 6

Summary of energy transfer during the second simulated heart beat under different LVAD flow protocols. KE is the total change in kinetic energy, PE is the total change in potential energy, work refers to total work performed through the cardiac cycle, energy output represents the total energy outputted over the boundaries (mitral, aortic and LVAD), while energy loss is the total energy lost via either boundary advection or viscous energy dissipation. All energies are in Joules.

	KE (J)	PE (J)	Work (J)	Energy output (J)	Energy loss (J)
L_{60}	-1.21×10^{-4}	7.71×10^{-4}	0.402	0.390	1.30×10^{-2}
L_{s60+}	-1.34×10^{-4}	1.08×10^{-3}	0.518	0.496	2.32×10^{-2}
L_{s60-}	-8.57×10^{-5}	4.54×10^{-4}	0.279	0.253	2.64×10^{-2}
L_{80}	2.60×10^{-4}	4.36×10^{-4}	0.338	0.311	2.71×10^{-2}
L_{s80+}	-1.31×10^{-4}	-3.86×10^{-4}	0.500	0.448	5.15×10^{-2}
L_{s80-}	-6.70×10^{-5}	-4.53×10^{-4}	0.149	9.35×10^{-2}	5.44×10^{-2}