Supplemental Material

Data S1.

A. Lumped parameter model

The lumped-parameter model (LPM) framework includes the following sub-models: 1) LV; 2) aortic valve; 3) aortic regurgitation and 4) systemic circulation (Figure 1, Tables 1 and 2). All input parameters were obtained from Doppler echocardiography measurements and brachial pressures in both pre and post intervention states. The model and sub-models have already been used and validated against *in vivo* cardiac catheterization (N=113) and *in vivo* MRI data (N=57) [1–6].

Heart-arterial model

The ventricle was filled by a normalized physiological mitral flow waveform adjusted for the required stroke volume. Coupling between left ventricle pressure and volume was performed through a time varying elastance E(t), a measure of cardiac muscle stiffness.

$$E(t) = \frac{P_{LV}(t)}{V(t) - V_0} \quad (1)$$

Where $P_{LV}(t)$, $V(t)$ and V_0 are left ventricular time-varying pressure, time-varying volume and unloaded volume, respectively. The amplitude of E(t) can be normalized with respect to maximal elastance E_{max}, *i.e.*, the slope of the end-systolic pressure-volume relation, giving $E_N(t_N)=E(t)/E_{max}$. Time then can be normalized with respect to the time to reach peak elastance, T_{Emax} ($t_N=t/T_{Emax}$).

$$E_{\max} E_N(t / T_{E\max}) = \frac{P_{LV}(t)}{V(t) - V_0} \quad (2)$$

As normalized curve of $E_N(t_N)$ can be described using Fourier series, therefore, the relation between $P_{LV}(t)$ and $V(t)$ can be determined for the left ventricle.

Modeling aortic valve

Aortic stenosis (AS) was modeled using Equation 3. This formulation expresses the instantaneous net pressure gradient across the stenotic valve (after pressure recovery) as a function of the instantaneous flow rate and the energy loss coefficient and links the LV pressure to the aorta pressure:

$$TPG_{net}\big|_{AS} = P_{LV}(t) - P_A(t) = \frac{2\pi\rho}{\sqrt{E_L Co\big|_{AS}}}\frac{\partial Q(t)}{\partial t} + \frac{\rho}{2E_L Co\big|_{AS}^2}Q^2(t) \tag{3}$$

and

$$E_L Co\big|_{AS} = \frac{(EOA\big|_{COA})A}{A - EOA\big|_{AS}} \tag{4}$$

where $E_L Co\big|_{AS}$, $EOA\big|_{AS}$, A, ρ and Q are the valvular energy loss coefficient, the effective orifice area, ascending aorta cross sectional area, the fluid density and the transvalvular flow rate, respectively. Variable aortic valve resistance (R_{av}) and constant aortic valve inductance (L_{av}) in the LPM are $\frac{\rho}{2E_L Co\big|_{AS}^2}Q(t)$ and $\frac{2\pi\rho}{\sqrt{E_L Co\big|_{AS}}}$, respectively.

Modeling aortic valve regurgitation

Aortic regurgitation (AR) was modeled using the same formulation as aortic stenosis. AR pressure gradient is the difference between aortic pressure and LV pressure during diastole.

$$TPG_{net}\big|_{AR} = \frac{2\pi\rho}{\sqrt{E_L Co\big|_{AR}}}\frac{\partial Q(t)}{\partial t} + \frac{\rho}{2E_L Co\big|_{AR}^2}Q^2(t) \tag{5}$$

and

$$E_L Co\big|_{AR} = \frac{(REOA)A_{LVOT}}{A_{LVOT} - REOA} \tag{6}$$

where $E_L Co|_{AR}$, $REOA$ and A_{LVOT} are regurgitation energy loss coefficient, regurgitant effective orifice area and LVOT area, respectively. Variable aortic valve regurgitation resistance (R_{av}) and constant aortic valve regurgitation inductance (L_{av}) in model are $\frac{\rho}{2E_L Co|_{AR}^2} Q(t)$ and $\frac{2\pi\rho}{\sqrt{E_L Co|_{AR}}}$, respectively.

Determining arterial compliance and peripheral resistance

The total systemic resistance was computed as the quotient of the average brachial pressure and the cardiac output (assuming a negligible peripheral venous pressure (mean ~ 5 mmHg) compared to aortic pressure (mean ~ 100 mmHg). This total systemic resistance represents the electrical equivalent resistance for all resistances in the current model. Because what the left ventricle faces is the total systemic resistance and not the individual resistances, for the sake of simplicity we considered the aortic resistance, R_{ao}, and systemic vein resistance, R_{SV}, as constants and adjusted the systemic artery resistance, R_{SA}, according to the obtained total systemic resistance.

For each degree of hypertension, we fit the predicted pulse pressure to the actual pulse pressure (known by arm cuff sphygmomanometer) obtained from clinical study by adjusting compliances (aorta (C_{ao}) and systemic (C_{SAC})).

Computational algorithm

The lumped parameter model was analyzed numerically by creating and solving a system of ordinary differential equations in Matlab Simscape (MathWorks, Inc.), enhanced by adding additional codes to meet demands of cardiac model in circuit. A Fourier series representation of an experimental normalized elastance curve for human adults was used to generate a signal to be fed into the main program (1,2,3,4). Simulations start at the onset of isovolumic contraction. Left ventricle volume, V(t), is calculated using left ventricle pressure, P_{LV}, and time varying elastance values (equation 1). Matlab's ode23t trapezoidal

rule variable-step solver was used to solve system of differential equations with initial time step of 0.1 milliseconds. The convergence residual criterion was set to 10^{-5} and initial voltages and currents of capacitors and inductors set to zero.

B. Computational fluid mechanics model

In this study, blood flow simulations rely on three dimensions fluid-solid interaction (FSI) computational fluid dynamics using FOAM-Extend [7] in which the system of equations governing the FSI problem are formulated using the finite volume method.

Governing equations for fluid domain

Blood flow was governed by the 3D incompressible Navier-Stokes equations and assumed to be a Newtonian and incompressible with a dynamic viscosity of 0.004 Pa·s and a density of 1060 kg/m^3 [8]. Continuity and momentum equations were as the following:

$$\iint_s (n.v)ds = 0 \tag{7}$$

$$\int_\forall \frac{\partial v}{\partial t} d\forall + \iint_s v[n.v]ds = \frac{1}{\rho}\iint_s n.[\mu \nabla v]ds - \frac{1}{\rho}\int_\forall \nabla p d\forall \tag{8}$$

where n is the normal vector to the surface S, V is the fluid velocity, μ is the fluid dynamic viscosity, P is the blood pressure and ρ is the fluid density. Due to the moving boundary of the fluid-solid interface, momentum equation (8) was considered in the form of Arbitrary Lagrangian-Eulerian (ALE) as follows:

$$\int_\forall \frac{\partial V}{\partial t} d\forall + \iint_s n.(v - v_s)vds = \frac{1}{\rho}\iint_s n.[\mu \nabla v]ds - \frac{1}{\rho}\int_\forall \nabla p d\forall \tag{9}$$

$$\frac{d}{dt}\int_\forall d\forall = \iint_s n.v_s ds \tag{10}$$

where V_s is the velocity of surface. Equation (10) indicates that the rate of changes of the volume and velocity of surface are in equilibrium.

Governing equations for solid domain

Because during diastole, the LV is passive its deformation depends on the tissue structure and the blood pressure inside the LV [9]. In this study, we developed a method to adjust patient-specific passive material properties of the LV for patients who undergo TAVR, based on our patient-specific DE-based LPM algorithm [1–6]. LV tissue was assumed to be an isotropic Saint Venant-Kirchhoff solid [10–15]. We adjusted the ventricular non-linear material properties during diastole using the results of our LPM algorithm as follows. The LPM algorithm provided the diastolic pressure as well as the pressure-volume (P-V) diagram. We applied the diastolic pressure as the boundary condition at the inner wall of the LV and by assuming different values for material properties, we obtained a series of P-V diagrams. Material properties were then interpolated to find the best value that can match the P-V results obtained using solid modeling to those obtained using the LPM.

According to the linear momentum conservation law in the total Lagrangian form, deformation of elastic and compressible solid were considered as the following:

$$\int_{V_0} \rho_0 \frac{\partial}{\partial t}(\frac{\partial u}{\partial t})dV = \iint_{s_0} n.(\Sigma.F^T)ds + \int_{V_0} \rho_0 b dV \tag{11}$$

where the subscript 0 describes the undeformed configuration and u is the displacement vector. F is the deformation gradient tensor and can be described as:

$$F = I + (\nabla u)^T \tag{12}$$

where I is the second order Identity tensor. Also, Σ in eq. (11) is the second Piola-Kirchhoff stress tensor and was described through Cauchy stress tensor (σ) as the following:

$$\sigma = \frac{1}{\det F} F.\Sigma.F^T \tag{13}$$

Using St. Venant-Kirchhoff constitutive material model, Σ was explained through isotropic Hooke's law:

$$\Sigma = 2\mu E + \lambda tr(E)I \tag{14}$$

where μ and λ are the Lame's constants (related to the Young's modulus and Poisson's ratio of material). E is the Green-Lagrangian strain tensor and is defined as follows:

$$E = \frac{1}{2}[\nabla u + (\nabla u)^T + \nabla u.(\nabla u)^T] \tag{15}$$

Fluid-structure interaction (FSI)

The fluid and solid solvers were coupled together to simulate the LV under pathophysiological flow and pressure conditions. Both solid and fluid were modeled using finite-volume approach. Fluid and solid solvers were coupled by kinematic and dynamic conditions for the LV. To satisfy the kinematic condition, the velocity and the displacement must be continuous across the interface [7]:

$$u_{f,i} = u_{s,i} \tag{16}$$

$$V_{f,i} = V_{s,i} \tag{17}$$

where subscripts i, s and f indicate the interface, solid and fluid regions, respectively. To satisfy the dynamic condition, the forces at the interface must be in equilibrium:

$$n_i.\sigma_{f,i} = n_i.\sigma_{s,i} \tag{18}$$

The Dirichlet-Neumann procedure at the interface indicates that fluid domain is solved for a given velocity/displacement and solid is solved for a given traction [7].

Boundary conditions & material properties

We used our patient-specific LPM (Figure 1) [1–5] : (1) to provide the time-dependent trans-mitral blood velocity; (2) to set the pressure, inside the LV; (3) to calculate material properties (see section Governing equations for solid domain). All geometries were reconstructed based on images at the beginning of diastole and, because PVL occurs in the left ventricular filling phase, all simulations were performed during diastole. Therefore, the TAVR was modeled to be rigidly closed and the mitral valve was modeled fully opened during the diastolic phase. The boundary surfaces between the fluid and solid inside the LV was considered as Moving wall boundary condition [15,16]. During diastole, there is an inflow from the atrium to the LV but there is no outflow from the LV due to the closed aortic valve. Since the blood is incompressible, interactions between the solid and fluid domains should be considered to allow the blood to expand and contract the LV wall to conserve mass. In order to solve the FSI problem inside the nonlinearly deforming LV, we used the Robin boundary condition for pressure based on the approach proposed by Tukovic et al [17].

Reconstructed geometries in patients with TAVR using CT images

We used CT images from patients with TAVR to segment and reconstruct the 3D geometries of the complete ventricle (ventricle, TAVR, coronaries, mitral valve and left atrium) using ITK-SNAP (version 3.8.0-BETA), a 3D image processing and model generation software package (Figure 1). These 3-D reconstructions were used for investigating hemodynamic using computational fluid dynamics.

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