Mechanics of left ventricular relaxation, early diastolic lengthening, and suction investigated in a mathematical model

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Submitted 18 February 2010; accepted in final form 8 February 2011

Remme EW, Opdahl A, Smiseth OA. Mechanics of left ventricular relaxation, early diastolic lengthening, and suction investigated in a mathematical model. Am J Physiol Heart Circ Physiol 300: H1678–H1687, 2011. First published February 11, 2011; doi:10.1152/ajpheart.00165.2010.—We investigated the determinants of ventricular early diastolic lengthening and mechanics of suction using a mathematical model of the left ventricle (LV). The model was based on a force balance between the force represented by LV pressure (LVP) and active and passive myocardial forces. The predicted lengthening velocity (e) from the model agreed well with measurements from 10 dogs during 5 different interventions (R = 0.69, P < 0.001). The model showed that e was increased when relaxation rate and systolic shortening increased, when passive stiffness was decreased, and when the rate of fall of LVP during early filling was decreased relative to the rate of fall of active stress. We first defined suction as the work the myocardium performed to pull blood into the ventricle. This occurred when contractile active forces decayed below and became weaker than restoring forces, producing a negative LVP. An alternative definition of suction is filling during falling pressure, commonly believed to be caused by release of restoring forces. However, the model showed that this phenomenon also occurred when there had been no systolic compression below unstressed length and therefore in the absence of restoring forces. In conclusion, relaxation rate, LVP, systolic shortening, and passive stiffness were all independent determinants of e. The model generated a suction effect seen as lengthening occurring during falling pressure. However, this was not equivalent with the myocardium performing pulling work on the blood, which was performed only when restoring forces were higher than remaining active fiber force, corresponding to a negative transmural pressure.

left ventricular lengthening velocity; predicted lengthening velocity; filling; tissue Doppler imaging

The mechanics governing early diastolic lengthening of the left ventricle (LV) and the concept of ventricular suction are not fully understood. This includes the influence of relaxation rate, filling pressure, restoring forces, and passive myocardial stiffness on ventricular lengthening and suction. Experimental and human studies (10, 13, 18, 19, 27, 26) have shown an empirical relation between LV longitudinal early diastolic lengthening velocity (e) and the following variables: relaxation rate, filling pressure, and restoring forces. However, a theoretical description explaining the physical laws that link these variables has not been developed. Such a mathematical model could help our understanding of the physics behind LV lengthening and suction.

Previously, Riordan and Kovacs (16) presented a mathematical spring-mass-damper model in a study of the longitudinal early diastolic lengthening velocity wave. They estimated the parameters in the model by fitting the calculated lengthening velocity wave to measurements from healthy and diabetic subjects and found significant differences in the model parameters between the two groups. However, their model did not take into account the effect of LV pressure (LVP) or relaxation of active fiber stress. Additionally, a prerequisite for lengthening to occur in their model was that it had been compressed below resting length. In a recent experimental study (13), we investigated the determinants of e. We confirmed previous findings (10, 18) that e was reduced at slowed relaxation, where the relaxation rate was evaluated through the exponential time constant (τ) of LVP decay during isovolumic relaxation (IVR) (22). Additionally, we found that e increased with increased restoring forces and increased transmural LVP at the time of mitral valve opening (MVO), termed lengthening load. Hence, our experimental study showed that the relaxation rate of active fiber stress, restoring forces, and lengthening load are variables that should all be included in a model of LV early diastolic lengthening.

The main general objective of this study was to investigate the mechanics of LV lengthening and diastolic suction by developing a mathematical simulation model. The model was validated by comparing the calculated e with measured e from our previous experimental study (13) using measured values for the model parameters.

The first of the two specific objectives of this study was to investigate the determinants of e and examine how variation of the different variables in the model affected e. A comparison was performed of the relationship between e and its determinants obtained from the mathematical model, which was based on the laws of physics, with the empirically obtained relationship from our experimental study (13). The experimental study indicated that changes in the relaxation rate changed the influence of restoring forces on e. The interaction between relaxation and restoring forces was explored in the model.

The second of the two specific objectives of this study was to clarify the role of restoring forces in the generation of suction for different definitions of suction. The concept of suction has been debated for a long time (2) and is still debated (17, 24). We applied the model to investigate and discuss the following three definitions of suction:

1. Generation of a negative transmural LVP.
2. Filling during falling pressure (7).
3. As an aspiration effect where the pressure is lowered in a chamber (LV) relative to a reservoir [left atrium (LA)]. Lowering of the chamber pressure creates the pressure difference that generates the flow from the reservoir into the chamber.

There is a common conception that suction is created by the release of restoring forces and that “the LV fills itself” by sucking

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blood from the LA. Using the model, we demonstrate that the phrase that “the LV fills itself” by suction is ambiguous as suction according to definitions 2 and 3 may occur even when the LV wall performs work opposing (pushing against) the inflow of blood to the ventricle. We show that the myocardium performs work to pull blood into the ventricle only when its transmural pressure is negative (definition 1) (1). Furthermore, we demonstrate that suction according to definitions 2 and 3 may be generated in the absence of restoring forces.

We divided the description of this study into the following four parts:
1. Description of the mathematics of the model.
2. Validation of the model.
3. Investigation of the proposed determinants of $e'$.
4. Investigation of the mechanics of suction and its relation to restoring forces.

**METHODS**

**Mathematical Model of LV Relaxation**

Myocardial force is a sum of active and passive (restoring) forces. Active force is caused by actin-myosin cross-bridge cycling, whereas passive myocardial force is caused by deformation of the elastic myocardial material from its unstressed resting state. The LV wall is also exposed to forces exerted by the LV cavity pressure and extraventricular structures [i.e., the pericardium, lungs/chest wall, and right ventricle (RV)], viscous, inertial, and gravitational forces, and a force at its attachment to the valve plane, which results from deformation of the elastic tissue in the atrium and aorta.

We modeled the LV myocardium in a simplified manner, applying a one-dimensional spring type model, including an active element, to represent the myocardium. A schematic of the model is shown in Fig. 1. It consisted of two elements in parallel representing active and passive elastic forces. Initially, all other forces were ignored in the model except the force represented by the ventricular pressure. The pericardial pressure was assumed to be zero in the model, so the ventricular pressure was equivalent to the transmural pressure. Equation 1 shows Newton’s third law for this model, where $S_A$ is active fiber stress, $S_P$ is passive elastic stress, $P$ is pressure, $t$ is time, and $A$ is the cross-sectional area of the spring, which may be cancelled out in this one-dimensional model:

$$[S_A(t) + S_P(t)] \cdot A = P(t) \cdot A$$

$$S_A(t) + S_P(t) = P(t)$$  \quad (1)$$

The chosen sign convention in Eq. 1 is that a positive pressure stretches the spring, whereas a positive active or passive stress seeks to shorten the spring. The passive properties of the myocardium were approximated as linear-elastic, and Hooke’s law was used to calculate $S_P$ as a function of the stiffness parameter ($K$), current myocardial length ($L$), and resting (i.e., unstressed) length ($L_0$):

$$S_P(t) = K \cdot (L(t) - L_0)$$  \quad (2)$$

By combining Eqs. 1 and 2, $L$ was found as follows:

$$L(t) = \frac{1}{K} [P(t) - S_A(t)] - L_0$$  \quad (3)$$

e’ was found as the time derivative of $L$ as follows:

$$e'(t) = \frac{dL(t)}{dt} = \frac{1}{K} \left[ \frac{dP(t)}{dt} - \frac{dS_A(t)}{dt} \right]$$  \quad (4)$$

Equation 4 shows that lengthening velocity is a function of the difference between the rate of pressure change and the rate of active stress change in this model. When pressure and active stress decay at the same rates, no change of dimension occurs, which represents the situation during IVR, ignoring isovolumic shape changes. For lengthening to occur, pressure must fall at a slower rate than active stress, i.e., $dP/dt$ must be less negative than $dS_A/dt$.

In our model, we prescribed the pressure and relaxation rate. Commonly, the relaxation rate is evaluated through the exponential time constant ($\tau$) of the pressure decay during IVR, i.e., slowing of the relaxation corresponds to an increase of $\tau$. If we assume that no deformation occurs during IVR ($S_P$ is constant), $S_A$ will decay exponentially during IVR. Pressure and $S_A$ differ by $S_P$ (Eq. 1), and, during IVR, pressure will decay exponentially toward an asymptote equal to $S_P$, whereas $S_A$ decays toward a zero asymptote. We assumed a continued exponential decay of active fiber stress to zero after MVO (5, 8). Calculations were started ($t = 0$) at MVO at a given LVP ($P_{MVO}$) and minimum length ($L_{min}$). $S_A$ at MVO ($S_{A,MVO}$) was calculated based on the equilibrium of forces in Eq. 1 as follows:

$$S_{A,MVO} = P_{MVO} - K \cdot (L_{min} - L_0)$$  \quad (5)$$

Equation 6 shows the exponential decay of $S_A$ as follows:

$$S_A(t) = S_{A,MVO} e^{-t/\tau}$$  \quad (6)$$

After MVO, pressure continues to decrease, but filling from the atrium elevates the ventricular pressure relative to the extrapolation of the exponential decay during IVR. We modeled the pressure fall during early filling as a continued but slowed exponential fall to a higher minimum value ($P_{min}$) than the asymptote it approached during IVR and with a different time constant ($\tau_F$) (Eq. 7). We assumed that lengthening started at MVO, i.e., $e' = 0$ cm/s at $t = 0$, thus ignoring any isovolumic shape changes before MVO. Hence, as shown in Eq. 4, the rate of $S_A$ decay was set equal to the rate of pressure decay (i.e., $dS_A/dt = dP/dt$) at MVO to fulfill the constant length condition.

Equation 8 shows the equal decay rates (time derivatives) of pressure and $S_A$ at the time of MVO assuming an exponential decay of these variables at this instance. $\tau_F$ was calculated as shown in Eq. 9, which ensured that the pressure trace was continuous and had a continuous derivative at MVO (i.e., a smooth transition) with respect to its exponential pressure decay during IVR:

$$P(t) = (P_{MVO} - P_{min})e^{-t/\tau_F} + P_{min}$$  \quad (7)$$

$$- \frac{(P_{MVO} - P_{min})}{\tau_F} = - \frac{S_{A,MVO}}{\tau}$$  \quad (8)

Fig. 1. Model of the left ventricular (LV) wall. The total wall stress is a sum of active myofiber stress ($S_A$) and passive elastic wall stress ($S_P$) modeled as two elements in parallel. The total wall stress is in equilibrium with the externally applied stress, which is measured in terms of pressure (P). Passive elastic wall stress (restoring forces) is modeled as a spring with length ($L$) equal to the current length of the wall.
The time-varying spring length and lengthening velocity in Eqs. 3 and 4, respectively, were calculated by inserting the equations for active fiber stress and pressure (Eqs. 6 and 7).

Model Validation

A comparison between predicted $e'$ from the simulation model with measurements from our previous animal study (13) was performed. In the previous experimental study, we performed recordings in 10 anesthetized, open-chest dogs during baseline, caval constriction, volume loading, infusion of dobutamine, and 15 min of ischemia induced by occluding the left anterior descending coronary artery. From sonomicrometry and pressure measurements in these dogs, we derived $P_{MVO}$ and $P_{min}$: unstressed longitudinal LV diameter ($L_0$), calculated as the diameter at a transmural LVP of zero; minimum diameter before MVO ($L_{min}$); $K$, calculated as the slope of linear regression of the end-diastolic LVP-diameter relation during caval constriction; and $\tau$, calculated as the time constant of the exponential LVP decay during IVR (starting 5 ms after minimum $dP/dt$ until 5 mmHg above $P_{MVO}$), assuming an asymptote equal to restoring forces, i.e., $K(L_{min} - L_0)$. Hence, all parameters required in the simulation model were obtained from the measurements. These parameters were extracted for each of the 10 animals for each of the 5 interventions together with measured $e'$. This resulted in 47 sets of measurements as 3 data sets were incomplete. For each of these 47 data sets, the measured parameters were used as input in the mathematical model, and $e'$ was calculated and compared with the corresponding measured $e'$.

Determinants of $e'$

The interventions in the experimental study were performed to vary the proposed determinants of $e'$ and investigate their effect on $e'$. One problem with the interventions was that they tended to change more than one of the proposed determinants at the time, making it more difficult to find the independent contribution of each determinant on $e'$. In the mathematical model, the investigation of the isolated effect of each determinant on $e'$ was performed in a more controlled manner. In the simulation model, we changed one determinant at a time and assessed its effect on $e'$. The other model parameters were kept at the baseline values, as shown in Table 1, which were the average values from the baseline recordings in the 10 dogs. When lengthening load was varied, both $P_{MVO}$ and $P_{min}$ were changed. From the experimental data, we observed that the difference between $P_{MVO}$ and $P_{min}$ decreased when $P_{MVO}$ was lowered. By a linear regression of the 47 data sets of measured $P_{MVO}$ and $P_{min}$, we found that $P_{min} = 0.67P_{MVO} - 2.74$ mmHg ($R = 0.89$). $P_{min}$ was varied with $P_{MVO}$ according to this formula when we investigated the effect of lengthening load on $e'$.

The resulting variation in peak $e'$ was plotted against the variation of each proposed determinant. In the same plot, the measurements from the experimental study were included for comparison.

In the experimental study, we found a significant interaction term between restoring forces and $\tau$ in their relation to $e'$, i.e., the slope of the relationship between a variation of restoring forces and the resulting variation in $e'$ was different at high and low values of $\tau$. We tested this in the mathematical model, where we investigated the relationship between $e'$ and $L_{min}$ at various levels of $\tau$ between 25 and 100 ms.

Mechanics of Suction

We applied the mathematical model to investigate the following different definitions of suction.

Suction: negative pressure (definition 1). The relationships between restoring forces, $S_a$, and pressure were first studied during the introduction of a negative LVP during early filling/lengthening. The typical LVP trace during this phase initially decays to a minimum pressure followed by a rise in pressure as it approaches its approximately static level at diastasis. We chose a parabolically shaped pressure trace (Eq. 10) to simulate a representative pressure trace that decreased from $P_{MVO} = 10$ mmHg to $P_{min} = -3$ mmHg in $t_{min} = 45$ ms, with a subsequent symmetrical pressure rise after $P_{min}$:

$$P(t) = a(t - t_{min})^4 + b(t - t_{min})^2 + P_{min}$$

where $a$ is and $b$ is. The pressure trace during filling must be consistent with an exponentially decaying pressure before MVO, i.e., it must be continuous and have a continuous time derivative at the time of MVO ($t = 0$). The parameters $a$ and $b$ were calculated so that Eq. 10 fulfilled these requirements. Generation of a negative pressure during filling is seen during increased contractility, which is associated with more systolic shortening and faster relaxation. Hence, for this simulation case, $L_{min}$ was reduced to 8% shorter than $L_0$ and $\tau$ was reduced to 35 ms, whereas passive stiffness was set equal to the baseline value. The resulting pressure trace is shown in Fig. 6, top left. A negative cavity pressure is associated with a negative endocardial surface tension, i.e., the surface traction vector is directed outward. Thus, the negative pressure represents a myocardial force that works in the direction of pulling blood into the ventricle. Hence, by requiring a negative pressure in the definition of suction, suction may be defined as the work the myocardial wall does on the blood by pulling it into the ventricle. This work was quantified as the pressure-length loop area below the 0-mmHg line.

Suction: filling during falling pressure (definition 2). Filling during falling pressure has been proposed as a sign of LV suction. It has been argued that for suction to arise, there must be intrinsic restoring forces in the wall that seek to expand the volume (or length in the one-dimensional case) (17, 25). This requires a contraction below $L_0$. We investigated if the phenomenon of lengthening during falling pressure was present in our model despite no systolic shortening below $L_0$ ($L_{min} > L_0$).

Suction: aspiration effect (definition 3). Applying the definition of suction as the ability of the LV to lower its pressure below LAP, i.e., an aspiration effect, we quantified a work analog performed by suction as the area of the LV-LA pressure-length loop below the LV-LA zero-pressure axis during early filling. The rationale for quantifying work in this manner is that work may be calculated as applied force times displacement. LAP represents a force that pushes blood into the LV, and positive LVP represents a force that pushes blood out of the LV. Hence, the net applied force in the direction of inflow is the LA-LV pressure difference. In the three-dimensional ventricle, the pressure difference would perform work by moving a volume of blood equal to the LV volume expansion; however, in our one-dimensional model, the volume expansion was replaced by lengthening. As suction defined by aspiration is the LV’s ability to lower its pressure below LAP, we limited the suction period to the

Table 1. Baseline parameter values obtained as the average from 10 animals during baseline conditions in the experimental study (13)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\tau$, ms</td>
<td>41</td>
</tr>
<tr>
<td>$P_{MVO}$, mmHg</td>
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</tr>
<tr>
<td>$P_{min}$, mmHg</td>
<td>4.2</td>
</tr>
<tr>
<td>$L_0$, mm</td>
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</tr>
<tr>
<td>$L_{min}$, mm</td>
<td>54.2</td>
</tr>
<tr>
<td>$K$, mmHg/m</td>
<td>2600</td>
</tr>
</tbody>
</table>

$\tau$, Time constant; $P_{MVO}$, left ventricular (LV) pressure at the time of mitral valve opening (MVO); $P_{min}$, minimum LV pressure; $L_0$, unstressed longitudinal LV diameter; $L_{min}$, minimum longitudinal diameter length before MVO; $K$, operating stiffness.
initial filling phase when LVP is lower than LAP. This corresponds to the phase from first pressure crossover at MVO when LVP falls below LAP until the second pressure crossover when LVP that has stopped decaying or is rising. In the model, LVP was prescribed to decay exponentially from PMVO to P_{min} as shown in Eq. 7, whereas LAP was prescribed to decay linearly from PMVO to P_{min} in 100 ms. The resulting pressure traces are shown in Fig. 8. The calculations were performed for both L_{min} < L_0 and L_{min} > L_0 with the other model parameters as shown in Table 1.

RESULTS

Model Validation

The measured variation in e' in the 47 data sets from the animal study was captured well by the simulation model. The resulting correlation plot is shown in Fig. 2, left. The overall correlation was \( R = 0.69 \) (\( P < 0.001 \)). The mean difference between the simulation model and measured e' was 0.0 \( \pm 1.6 \) cm/s, as shown in the Bland-Altman plot in Fig. 2, right. The points in Fig. 2 are labeled according to each experimental intervention. The three cases where the model overestimated e' the most were the three cases with the lowest measured K and relatively large compression below L_0. The majority of the cases with the most underestimated e' occurred during volume loading. There were no systematic error in the range of measured e', but the SD increased for larger values of e', and two cases deviated outside \( \pm 1.96 \) SD.

Determinants of e'

Example traces from simulation cases with isolated variations of one variable at a time are shown in Fig. 3. The relationships of each separate determinant and e' are shown in Fig. 4, where the experimental measurements are also included. Slowing the relaxation rate by increasing \( \tau \) reduced and delayed e' (Figs. 3A and 4A). Increased pressure during filling increased e' (Figs. 3B and 4B). Simulations with reduced end-systolic length increased restoring forces and increased e' (Figs. 3C and 4C). Increasing passive elastic wall stiffness decreased e' (Figs. 3D and 4D). There was no experimental equivalent to the simulation case altering passive stiffness.

The results showed an interaction effect between relaxation rate and restoring forces on their influence on e'. At slowed relaxation, the effect of restoring forces on e' was substantially reduced compared with that at fast relaxation. The results shown in Fig. 5 demonstrate that during rapid relaxation, e' was highly dependent on the degree of restoring forces: at \( \tau = 25 \) ms, e' increased by 15 cm/s when L_{min} relative to L_0 (L_{min} − L_0) was changed from +1 to −5 mm. However, at \( \tau = 100 \) ms, the increase of e' was reduced to 4 cm/s for the same change of shortening. The simulation results were consistent with a similar trend observed in our experimental study (13).

Fig. 2. Comparison between calculated lengthening velocity (e') from the simulation model with the corresponding measured e' from the animal study (13). Left: a correlation plot; right: corresponding Bland-Altman plot. Data from 10 animals during 5 different interventions were included, and the compared pairs of e' are labeled according to the intervention: baseline (B), caval constriction (C), dobutamine infusion (D), ischemia (I), and volume loading (L).

Fig. 3. Simulation results from varying the different model parameters in turn. Simulation using baseline parameter values (Table 1) are shown with solid lines, whereas increased values of each of the model parameters [time constant (\( \tau \)), pressure at mitral valve opening (PMVO) and minimum pressure (P_{min}), minimum length (L_{min}), and stiffness parameter (K)] are shown by a dashed line and reduced values with a dotted line. In A, \( \tau \) was increased and decreased to 70 and 25 ms, respectively. In B, PMVO and P_{min} (lengthening load) were increased to 13 and 7 mmHg, respectively, and decreased to 7 and 1 mmHg, respectively. In C, L_{min} was increased and decreased to 55.2 and 53.2 mm, respectively. In D, K was increased and decreased to 3,600 and 1,600 mmHg/m, respectively.

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Mechanics of Suction

Suction: negative pressure. Figure 6 shows the results from the simulation case where a negative pressure was generated during early filling. The moment the contractile active stress became weaker than $S_P$, acting in the opposite direction to lengthen the structure, the pressure became negative. The pressure remained negative while $S_P$ was stronger. Hence, the net wall stress worked in an expanding direction, and the myocardium performed work, extending itself (Fig. 6, right).

Suction: filling during falling pressure. The mathematical model showed that lengthening occurred during falling pressure even when $L_{\text{min}}$ was above $L_0$ (Fig. 7). Hence, this phenomenon was in that case not caused by the release of restoring forces but a result of the ongoing relaxation.

Suction: aspiration effect. Defining suction as the aspiration effect, suction work was performed when $L_{\text{min}}$ was below or above $L_0$. However, suction work was larger when $L_{\text{min}}$ was shorter than $L_0$ due to more lengthening occurring, as it represented a more compliant ventricle than when $L_{\text{min}}$ was longer than $L_0$ (Fig. 8, right). While this suction work was performed by the LA-LV pressure difference, the work performed by the LA-LV pressure difference, the work per-
formed by the myocardial wall itself was the sum of the work performed by $S_p$ and $S_A$. In both simulation cases, the sum of these stresses acted in a contractile direction opposing lengthening. Hence, the muscle was lengthened by the external LVP while the myocardium generated $S_A$ opposing lengthening. In skeletal muscle physiology, this situation is known as “eccentric contraction,” i.e., an external force stretches a muscle that generates an active contractile force (1a, 23a). Thus, the external force represented by the LVP performed work to lengthen the myocardium, whereas the myocardium performed eccentric (negative) work opposing lengthening.

**DISCUSSION**

In this study, we investigated the mechanics of LV early diastolic lengthening and suction in a mathematical model.

The main findings from the investigation of early diastolic lengthening were as follows:

1. The predicted $e'$ from the model agreed well with the corresponding measured $e'$ in 10 animals during 5 different interventions.

2. The model showed that $e'$ was increased by the following alterations of its determinants:
   a. Faster relaxation of active myofiber stress.
   b. When LVP (lengthening load) decreased more slowly than $S_A$.
   c. Decreased end-systolic length.
   d. Decreased passive stiffness.

3. Slowing of relaxation reduced the effect of restoring forces on $e'$.

The main findings from the investigation of suction were as follows:

1. The LV wall performed work to pull blood into the ventricle only in the presence of a negative transmural LVP.

2. Lowering of LVP below atrial pressure during filling (aspiration/suction) and filling during falling pressure also occurred when there had been no compression below $L_0$, demonstrating that suction, according to this definition, does not have to be caused by the release of restoring forces.

**Determinants of the Rate of LV Lengthening**

The model predicted $e'$ based on the variables $\tau$, $P_{MVO}$, $P_{min}$, $S_p$, $L_0$, and $L_{min}$. These parameters were measured in animals in 47 different cases, and the measured parameter values were used to calculate $e'$. The correlation between the model-predicted and measured $e'$ may be regarded as very good considering the uncertainties in the measurements and the simplicity of the model. The largest difference was seen for the volume-loading intervention, which particularly increased pressure. This may suggest that the mathematical description of the pressure in the model caused the largest discrepancies, and a more advanced pressure description could possibly improve the results. However, a more advanced mathematical description of the pressure curve requires more input parameters that must be measured, and, although it may improve the correlation, we believe it would not change our conclusions regarding the determinants of $e'$ and mechanics of suction.

Previous empirical studies (10, 13, 18, 19, 27, 26) have shown a relation between $e'$ and $\tau$, restoring forces, and lengthening load. However, our model suggests that it is not the load or pressure magnitude per se that determines $e'$ but the rate of change in pressure relative to the rate of change of active myofiber stress, as shown in Eq. 4; if they fall by the same amount, the wall will not lengthen or shorten as the external stretching force is reduced by the same amount as the internal myocardial contractile force. This is the case during IVR, when the dimension is constant. Only when the rate of fall of pressure is slowed down due to inflow from the LA will the wall experience a net expanding force as the active myofiber stress then falls at a quicker rate, and, hence, the LV will start lengthening. In the experimental study, we observed that a high $P_{MVO}$ resulted in a high $e'$. A high $P_{MVO}$ is associated with a high LAP, which normally indicates a higher ability of the LA to quickly supply the LV with blood during early filling. In that case, the LVP fall will be rapidly slowed down (i.e., $\text{dP}/\text{dt}$ less negative) due to rapid inflow and result in a higher $e'$. The mathematical model confirmed restoring forces as an independent determinant of $e'$ as a higher degree of shortening below $L_0$ produced higher restoring...
forces, which caused a higher lengthening velocity during relaxation.

The model showed that increased passive stiffness reduced $e'$, consistent with another modeling study (20) that showed decreased early diastolic blood flow velocity through the mitral valve with decreased ventricular compliance. This result may be intuitive for stretching above $L_0$ as a stiffer spring will lengthen less when the same stretching load is applied, and, hence, it will lengthen with a lower velocity than a more compliant spring. When a stiff spring and a more compliant spring are shortened by the same amount below $L_0$ during systole, the stiff spring will have higher restoring forces, which one might think would increase its lengthening velocity. However, active fiber stress must also be higher to compress the stiffer spring to the same degree. Relaxation is not an instantaneous process, and it takes longer to relax a higher $S_A$ than a lower $S_A$. Since the stiffer spring is at a higher $S_A$ level, it takes longer to reach zero $S_A$ compared with the more compliant spring. This is shown in Fig. 9. When the stiffer spring and the more compliant spring are lengthened by the same amount, the velocity will be slower for the stiffer spring as it takes longer to relax and to release the restoring forces. Relaxation works as a brake on the release of restoring forces: the slower relaxation, the slower the release of restoring forces. This was further illustrated in the simulation case with different relaxation rates: the increase of $e'$ was much lower when systolic shortening (and therefore restoring forces) was increased during slowed relaxation compared with fast relaxation, as shown in Fig. 5. Hence, slowing of relaxation reduced the effect of restoring forces. This finding was consistent with the finding of a significant interaction term between relaxation rate and restoring forces in our experimental study (13), where the slope of the relationship between the degree of systolic shortening and $e'$ was reduced at higher $\tau$ values.

### Mechanics of Suction

The model showed that for the LV myocardium to perform work to pull blood into the ventricle, restoring forces had to be stronger than active contractile forces, which occurred when pressure became negative (Fig. 6). The ventricular pressure is a result of wall tension. In the case that pericardial pressure is zero, the net myocardial wall tension is reflected at the endocardial surface as the surface traction vector (the tension along the vector normal to the surface). When the surface traction vector points into the ventricle, a positive pressure is generated. This situation can be caused by both active contractile forces or passive forces when the ventricle is extended above the equilibrium volume ($V_0$; defined as the LV volume at zero transmural pressure). Hence, this positive pressure represents a force that seeks to push blood out of the ventricle. If the active contractile forces become less than the expanding passive forces (restoring forces), the surface traction vector points outward (negative surface tension) (see Fig. 6, left). This generates a negative pressure and represents the situation when the myocardium generates a force that seeks to pull blood into the ventricle. Hence, the direction of the surface traction vector (assuming a zero pericardial pressure) or sign of the transmural pressure determines if the myocardium is doing pushing or pulling work on the blood. As long as the transmural pressure is positive, the LV myocardium will seek to push blood out of the ventricle; however, inflow of blood into the LV is still ensured as long as LAP is higher than LVP as the LA then pushes with a greater force. The LV creates an aspiration effect (suction) by lowering its push relative to the LA push, but decreasing the push does not mean the LV is pulling on the blood. The LV wall performs pulling work on the blood only if the transmural pressure is negative, whereas it is doing pushing work when it is positive, as shown in Fig. 6. Cheng et al. (3) measured negative LVPs in dogs during exercise and showed that increased early diastolic filling was generated by lowering of the LVP, whereas LAP was unchanged. The end-systolic volume was smaller on average and the relaxation rate was faster during exercise. This is consistent with our explanation that $S_A$ must fall below $S_P$ to generate a negative pressure, which may occur in a situation when there is significant compression below $V_0$ and relaxation occurs so fast that $S_A$ manages to fall below $S_P$ before expansion above $V_0$. After 4–5 wk of pacing-induced heart failure, the dogs lost the ability to generate negative pressure during exercise, as demonstrated by an increasing minimum LVP. This occurred simultaneously with increased LAP, slowed relaxation rate, and increased end-systolic volume (4).

Our model showed that lengthening could occur during falling pressure despite no compression below $L_0$. This was demonstrated when the spring model was initially longer than $L_0$ and still lengthened when pressure was decreased during relaxation (Fig. 7). Release of restoring forces can occur only when it has been compressed below $L_0$ ($L < L_0$, $S_P < 0$). Hence, lengthening during falling pressure was not caused by the release of restoring forces in that case. Lengthening occurred as a consequence of $S_A$ decaying faster than pressure, which may be interpreted as a sign that the ventricle relaxes faster than it can fill (23). Our model suggests that lengthening during falling pressure, in fact, is a result of ongoing relaxation. This is demonstrated by Eq. 3: if $S_A(t)$ is zero or

![Fig. 9. Top: passive stress levels $S_1$ and $S_2$ for a soft and stiff spring, respectively, at a given $L_{min}$ relative to $L_0$. Bottom: the time it takes to relax active stress from the higher stress level is longer ($\Delta t_2$) than the time it takes from the lower level ($\Delta t_1$). During relaxation, it will therefore take longer time for the stiff spring to lengthen, i.e., lower lengthening velocity, due to the longer time it takes to decrease the higher active stress.](image)
constant, then \( P(t) \) would have to increase for lengthening to occur. The only way for pressure to decay while the ventricle expands is if \( S_A \) decays faster.

Active contraction produces a high systolic pressure that is reduced during relaxation. As \( S_A \) decays toward zero, the ventricle will seek to reduce its pressure down to the pressure given by the current volume according to the ventricle’s passive pressure-volume characteristic. This is demonstrated in Fig. 10, which shows a passive LV pressure-volume characteristic similar to the findings of Nikolic et al. (11). They obtained the passive pressure-volume relationship by letting the ventricle relax completely at different end-systolic volumes by controlling filling. During relaxation, LVP will naturally decay toward its fully relaxed pressure at the current volume, as shown by the solid arrows in Fig. 10. Relaxation down to this pressure is interrupted by onset of filling. Inflow from the LA prevents the ventricle from reaching its fully relaxed pressure at its current volume. One may argue that filling during falling pressure is a sign that the LA supplies blood at a slower rate than the LV relaxes. However, unless LAP increases, LVP must decrease to generate an LA-to-LV pressure difference. Blood is pushed from the LA by the pressure difference. Hence, as long as the LAP is constant or decreases, the pressure in the LV must decrease below LAP to create a blood flow into the LV. As an alternative extreme situation, one could imagine that the ventricular pressure remained constant at \( P_{MVO} \). Unless LAP increased, there would be no flow generated between the LA and LV due to the lack of a pressure difference. In the absence of a pressure difference that pushes blood into the LV, it is still possible that the LV could lengthen in the long-axis direction due to relaxation and restoring forces. In this manner, the LV wall could move upward in the direction of the atrium and engulf stationary blood previously positioned inside the LA wall; hence, the LV volume would expand without the generation of a pressure difference and blood flow. The LV could not expand in the short-axis direction in a similar manner and engulf any stationary blood. Thus, a pressure difference must be induced for a short-axis expansion to occur, as blood would have to flow in to fill the increased space. The described principles of relaxation in relation to the pressure-volume relationship are in agreement with Katz’s demonstration (7) of LVP and volume relations in an isolated heart that was relaxing isometrically or nearly isotonically.

In this study, we propose a method to quantify the aspiration work, i.e., the work reflecting the LV’s ability to lower its pressure below atrial pressure. This work was quantified as the area under the zero-pressure axis of the LV-LA pressure difference versus length (volume) loop for the initial filling phase from MVO to the second LV-LA pressure crossover. Wang et al. (21) proposed a related work index as the energy in the backward expansion wave during the phase from MVO to minimum LVP. The duration of the two different work indexes may vary slightly as we include the phase after LVP has started to increase until it again equals LAP, which, in practice, is a very short period. However, our argument for also including this phase is that if suction should be defined as the ability of the LV to lower its pressure below LAP, we should include the entire period that the LV “is responsible” for the lower pressure and creating the LA-LV pressure difference that accelerates blood into the LV.

We stress that this pressure work index is not the same as the work the LV wall is doing. It resists inflow as long as the net wall forces create a positive transmural LVP. In this case, the blood is performing work on the LV wall, stretching it while the LV wall performs eccentric (negative) work, consuming energy. Practically, all hearts are capable of lowering their ventricular pressure below atrial pressure during early filling, including very sick, dilated hearts, which do not contract below unstressed volume. This is shown in Fig. 10 by the pressure-volume loop with a minimum volume above \( V_0 \) that seeks to reduce its pressure down to its fully relaxed pressure, which is below LAP. Typically, an elevated LAP and enlarged LA in diseased hearts assist the LV to aspirate blood from the LA in this manner.

A suction pump works by a piston creating a partial vacuum, which lowers the pressure in the pump relative to the reservoir so that fluid is pushed in from the reservoir to the other side (5a). As the LV has the ability to lower its pressure relative to the reservoir in the LA, it may be defined as a suction pump. Thus, one may say that the ventricle sucks blood from the atrium during early filling. However, this does not imply that the ventricular wall pulls blood into the ventricle. Only when restoring forces are larger than active forces will the wall perform work to pull blood into the ventricle, which occurs only when its endocardial surface tension is negative, i.e., when a negative transmural pressure is present.

**Limitations**

The developed mathematical model of LV relaxation, which consisted of only an active element and a passive element in parallel, is a gross approximation of the LV, representing it as a one-dimensional structure. It is a steady-state model disregarding inertial and viscous forces as well as forces exerted by gravity and extraventricular structures (i.e., the pericardium, lungs/chest wall, and RV) and a force at its attachment to the valve plane, which
results from deformation of the elastic tissue in the atrium and aorta. The real LV wall is three dimensional with regional inhomogeneities and goes through complex three-dimensional deformations during the cardiac cycle, including shear deformation. There might also be differences in how the long-axis and short-axis dimensions behave during early diastole. While the longitudinal e’ lengthening wave and the transmural E filling wave occur nearly simultaneously in the normal heart, it has been reported that during heart failure, e’ may be delayed relative to the E wave, suggesting an earlier expansion in the radial dimension than the longitudinal dimension (6). This phenomenon may be related to delayed apical filling and/or more spherically shaped ventricles compared with the more tapered shape of normal ventricles. More complex mathematical three-dimensional models including coupled fluid-wall interactions are required to study these phenomena. The simplified representation of the LV mechanics may be an advantage in certain respects as more people may be able to comprehend the simple physics of such a model and improve their understanding of LV mechanics. Extension of the model to also include inertial and viscous forces makes the model one step more realistic. However, this also increases its complexity, and advanced engineering mathematics is required to solve the model, which reduces accessibility and understanding. Another disadvantage is the introduction of more uncertainties with respect to the unknown parameters for mass and viscosity that must be included in the model. Since the main purpose of this study was to improve the understanding of early diastolic LV mechanics, we chose to apply a simple model excluding inertial and viscous forces. Due to the simplified nature of our model, considerable caution should be applied when translating the results to the real heart. However, we believe our simple model incorporates the major physical principles that are at work during early filling, and we believe it is likely that the same physical principles that apply to lengthening of this spring model in general also apply to the myocardium. This is supported by the good agreement between the model predictions and experimentally observed results.

The myocardial passive elastic properties were modeled using a linear stress-strain relationship. Although the true relationship is nonlinear, it may be approximately linear around L₀. We desired a model that qualitatively and simply could illustrate the effect of changes in passive elastic stiffness on e’, which was achieved with the one parameter in the linear stress-strain relationship. Incorporation of a more complex nonlinear relationship in the model is possible at the cost of introducing more model parameters and less comprehensible equations.

Other determinants of e’ may be considered to be LAP and the LV filling rate. However, we regard those as primarily determinants of LVP and that they indirectly determine e’ through LVP. The external expanding force represented by the pressure in our model may be viewed as transmural pressure, i.e., LVP minus pericardial pressure, as the pericardial pressure works as an external force restricting expansion, which should therefore be subtracted from the expanding LV cavity pressure.

It has been shown that even at a transmural LVP of zero there are residual stresses in the wall (12, 15). Our one-dimensional model does not include residual stresses. We apply the term “unstressed” length (L₀) or volume (V₀) as the dimension when zero external pressure and zero internal active stress is present. Hence, this is the length or volume to which the structure returns to at rest.

Conclusions

The developed mathematical model of LV relaxation physically links e’ to its determinants. The model showed that e’ is determined by relaxation rate of active fiber stress, LVP during early filling, restoring forces, and passive elastic wall stiffness. The model also suggested that filling during falling pressure is a result of ongoing relaxation and is not caused by the release of restoring forces. Suction has been defined both as the ability of the ventricle to lower its pressure below atrial pressure and as the generation of a negative transmural ventricular pressure. However, only the latter definition is consistent with the notion that the ventricular myocardium performs work to pull blood into the ventricle.

GRANTS

E. W. Remme and A. Opdahl were recipients of research fellowships from Helse Sw-Nst and the Norwegian Council on Cardiovascular Diseases, respectively.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

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