Fluid Dynamics Model of Mitral Valve Flow: Description With In Vitro Validation

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A lumped variable fluid dynamics model of mitral valve blood flow is described that is applicable to both Doppler echocardiography and invasive hemodynamic measurement. Given left atrial and ventricular compliance, initial pressures and mitral valve impedance, the model predicts the time course of mitral flow and atrial and ventricular pressure. The predictions of this mathematical formulation have been tested in an in vitro analog of the left heart in which mitral valve area and atrial and ventricular compliance can be accurately controlled.

For the situation of constant chamber compliance, the mitral gradient is predicted to decay as a parabolic curve, and this has been confirmed in the in vitro model with $r > 0.99$ in all cases for a range of orifice area from 0.3 to 3.0 cm$^2$, initial pressure gradient from 2.4 to 14.2 mm Hg and net chamber compliance from 16 to 29 cc/mm Hg. This mathematical formulation of transmitral flow should help to unify the Doppler echocardiographic and catheterization assessment of mitral stenosis and left ventricular diastolic dysfunction.

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ward validation of the fundamental equations underlying our text for details. All symbols defined in Table 1.

tricular compliance along with initial atrial and ventricular pressure; it returns, for output, the time course of mitral flow and chamber pressure. The specific pressure and flow predictions have a complex theoretic dependence on chamber compliance and mitral valve morphology, which have proved difficult at times to demonstrate in vivo, because available methods provide an imperfect measure of chamber compliance and valve impedance. Therefore, we have developed an in vitro model of the left heart in which chamber compliance, valvular morphology and initial pressures may be rigidly controlled. Pressure and flow are digitized at high speed and then compared with the specific predictions of the mathematic mitral flow model. We assume that a cylindric column of blood with length $l$, area $A$ and density $\rho$ is accelerated through the mitral valve by the pressure gradient between the left atrium and left ventricle. This blood column is actually just an imaginary boundary enclosing the blood rushing through the mitral valve and is roughly the dimensions of the mitral apparatus. This imaginary boundary does not move, only the blood contained within it. Therefore, the actual contents of the column are constantly changing, with new blood entering from the left atrium and an equal amount departing into the left ventricle. Such a stationary frame of reference within moving fluid is termed an Eulerian coordinate system and is very widely used in fluid dynamics problems. Therefore, when we speak of the velocity ($v$) of the blood column, we are actually referring to the blood velocity within the column. The acceleration ($a$) of this blood is $dv/dt$. (All mathematic symbols are explained in Table 1.)

The flow rate through the mitral valve ($q$) is given by $\nu A$.

We assume that the left atrium includes the pulmonary veins in a common chamber that receives the full stroke volume from the right ventricle in systole and discharges it by elastic recoil during diastole. The left atrium and ventricle are characterized by pressure and compliance relations that dictate the change in chamber pressure with changes in chamber volume.

**Derivation of the Equations of Motion**

**How is flow affected by chamber pressures?** Newton's second law of motion states that Force = Mass × Acceleration or (rearranging) Acceleration ($a$) = $F/m$, where $m$ is the mass of blood within the column boundary ($\rho A l$) and $F$ is the driving force across the mitral valve. It is convenient to consider flow acceleration rather than velocity acceleration by multiplying both sides by the cross-sectional area ($A$) yielding

$$\frac{d\nu}{dt} = Aa = F/\rho.$$

**Now consider the nature of the force $F$.** The most obvious component of this is the driving pressure difference between the atrium and the ventricle, $A(p_a - p_v)$. This forward force is counterbalanced by two components of hydraulic resistance. The first resistance term relates to the conversion of pressure into kinetic energy as the blood accelerates through the valve; termed convective resistance, it is proportional to the square of the blood velocity and is most familiar in the modified Bernoulli equation; its unit of proportionality is termed $R_c$. The second resistive force is due to viscous drag as blood passes through the valve and is proportional to the flow rate. It is most familiar in Poiseuille’s law for flow through narrow tubes and is termed $R_v$. In fact, as will be shown later, the effect of viscous resistance on mitral valve flow is very small and can be neglected for most clinical problems.

![Schematic Anatomy](image)

**Figure 1.** Schematic anatomy of lumped variable model of mitral flow consisting of two elastic chambers connected by a valve. The proximal chamber contains the left atrium and pulmonary veins and receives the full stroke volume from the right heart in systole; this blood is then discharged by elastic recoil through the valve into the left ventricle. The blood actually passing through the valve is considered to lie within an imaginary cylinder of area $A$ and length $l$, roughly the dimensions of the mitral apparatus. Mitral valve impedance contains two resistive components ($R_v$ and $R_c$) and one inertial term ($M$). The atrial and ventricular chambers are characterized by compliance relations, which may be functions of chamber pressure and (to allow for active ventricular relaxation) time. See text for details. All symbols defined in Table 1.

**Description of the Mathematic Model**

**Schematic Anatomy**

Figure 1 displays the schematic anatomy used for our mathematic mitral flow model. We assume that a cylindric column of blood with length $l$, area $A$ and density $\rho$ is accelerated through the mitral valve by the pressure gradient between the left atrium and left ventricle. This blood column is actually just an imaginary boundary enclosing the blood rushing through the mitral valve and is roughly the dimensions of the mitral apparatus. This imaginary boundary does not move, only the blood contained within it. Therefore, the actual contents of the column are constantly changing, with new blood entering from the left atrium and an equal amount departing into the left ventricle. Such a stationary frame of reference within moving fluid is termed an Eulerian coordinate system and is very widely used in fluid dynamics problems. Therefore, when we speak of the velocity ($v$) of the blood column, we are actually referring to the blood velocity within the column. The acceleration ($a$) of this blood is $dv/dt$. (All mathematic symbols are explained in Table 1.)

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situations. It is included here for mathematic completeness and to allow maximal generality of the flow model. These two forces, \( R, q^2 \) and \( R, q \), serve to offset the pressure gradient \( p_a - p_v \), and thus we can write an equation analogous to Newton’s second law as

\[
\frac{dq}{dt} = (p_a - p_v - R, q^2 - R, q)/M. \tag{1}
\]

where \( M \) is a distributed mass term, \( \rho A \) with units g-cm\(^{-4}\). Because \( dq/dt \) has units of cm\(^{-3}\)s\(^{-2}\), we can show that \( R, \) has units g-cm\(^{-4}\)s\(^{-1}\) and \( R, \) has units g-cm\(^{-7}\). We will later relate these terms (in an order of magnitude sense) to \( A, p \) and blood viscosity (\( \eta \)). First, however, we need equations to describe how atrial and ventricular pressure change with transmural flow.

**How are chamber pressures affected by flow?** We assume that at any point in time, left ventricular pressure is a function of left ventricular volume, \( p_v(V_v) \), and similarly, left atrial pressure is a function of atrial volume, \( p_a(V_a) \). (Note that here and throughout this report all references to the left atrium implicitly include the pulmonary veins because in our schematic model these are considered to be a common elastic chamber.) Chamber stiffness is defined as the change in pressure with volume, \( dp/dV \); its reciprocal is compliance, \( dV/dp \). Therefore, left atrial compliance \( (C_a) \) is \( dV_a/dp_a \) and ventricular compliance \( (C_v) \) is \( dV_v/dp_v \).

We seek expressions relating the rate of change in chamber pressure \( (dp/dt) \) to the flow into or out of that chamber. Recall that transmural flow \( (q) \) is the same as the rate of change in ventricular volume \( (dV_v/dt) \) and the negative of the rate of change in left atrial volume \( -(dV_a/dt) \). The chain rule for derivatives allows us to make the following observation:

\[
\frac{dp_v}{dt} = (dV_v/dt)/dV_v/dp_v = -q/C_a, \tag{2}
\]

\[
\frac{dp_a}{dt} = (dV_a/dt)/dV_a/dp_a = q/C_v. \tag{3}
\]

By convention we have written these equations as flow divided by compliance; multiplying flow by stiffness \( (dp/dV) \) would have been precisely equivalent.

For equations 2 and 3 as written to be correct, changes in chamber pressure must be mediated solely through changes in chamber volume. However, we will show below how equation 3 can be modified to model active ventricular relaxation, in which pressure drops even when there is no change in volume.

**Equations 1, 2 and 3 fully specify the behavior of our mathematic model:** equation 1 dictates how pressure affects flow; equations 2 and 3 dictate how flow affects chamber pressures. Taken together, they form a coupled system of nonlinear ordinary differential equations that can predict the time course of mitral flow and atrial and ventricular pressure, given known initial pressures \( (p_a[0] \text{ and } p_v[0]) \).

impedance \( (M, R_a, \text{ and } R_v) \) and chamber compliance curves \( (C_a[p_a] \text{ and } C_v[p_v, t]) \).

These three equations may be reduced to two coupled differential equations by making the substitutions \( \Delta p = p_a - p_v \), and

\[
C_n = (1/C_a + 1/C_v)^{-1} \approx C_C/(C_a + C_v), \tag{4}
\]

and subtracting equation 3 from equation 2 yields

\[
\frac{\Delta p}{dt} = -q/C_n. \tag{5}
\]

This more compact representation will be used in the analysis of the in vitro model later.

**Morphologic Determinants of Mitral Impedance**

It is useful to examine equations 1 and 4 in light of known hydrodynamic principles to estimate and give physical meaning to \( M, R_a, \text{ and } R_v \). We have already applied simple dimensional analysis to the inertial term and seen that \( M = \rho A \). To approximate \( R_a \) and \( R_v \), we consider the situation of steady state flow, that is, where \( dq/dt = 0 \) and the effect of \( M \) is eliminated. The goal of this “thought experiment” is simply to gain some insight into the physical meaning of \( R_a \) and \( R_v \); it matters little that true mitral flow is distinctly unsteady. In the more realistic circumstance, \( R_a \) and \( R_v \) should have the same values as in the steady state situation, with the additional effect of \( M \) factored in. Under the special situation of steady state flow, equation 4 becomes

\[
\Delta p = R_a q + R_v q^2. \tag{6}
\]

To separate the effect of \( R_a \) and \( R_v \) in this equation, we further consider experimental situations previously shown to be dominated by convection or viscosity, respectively.

**Hydrodynamic meaning for \( R_v \).** It has been shown (14) that the pressure drop for flow across a stenotic orifice in a thin plate is well approximated by the modified Bernoulli equation, with viscous effects neglected: \( \Delta p = \rho v^2/2 \), where \( v \) is the transmural velocity. This must be equivalent to equation 6 with \( R_v \) set to 0 (that is, \( \Delta p = R_a q^2 \)) and thus \( R_v q^2 = \rho v^2/2 \). Substituting \( v = -q/A \), this becomes \( R_v = \rho 2A^2 \).

We may also establish a correspondence between \( A \) and the anatomic valve area \( (MVA) \). This is simply \( c_v MVA \) and \( R_v \approx \rho 2(c_v MVA)^2 \). Note that \( c_v \) is not a constant but instead varies with valve shape.
and entry geometry. Thus, the precise relation between \( R_c \) and MVA must await empiric observation.

**Hydrodynamic meaning for \( R_c \).** Now consider a steady state flow situation where viscous resistance would be expected to dominate convective resistance, such as a long thin tube of area \( A \) and length \( l \) (16). Here the pressure drop is given by Poiseuille's equation \( \Delta p = 8 \eta A / \pi l^4 = 8 \eta \pi q / A^2 \), where we have substituted \( A = \pi l^2 \). This equation must be equivalent to that of equation 6 with \( R_c \) set to 0 (that is, \( \Delta p = R_q \)).

Simplified estimates for \( M, R_c \) and \( R_v \). By substituting for the known density and viscosity of blood, we obtain more compact representations for the components of mitral impedance (still quite approximate):

\[
M = \rho l / A = l / A \tag{7}
\]

\[
R_c = \rho / 2A^2 = 0.5 / A^2 \tag{8}
\]

\[
R_v = 8 \pi \eta / A^2 = 1 / A^2 \tag{9}
\]

**Anatomic interpretation of \( A \) and \( l \).** What values should be assigned to \( A \) and \( l \), the dimensions of the imaginary boundary enclosing the blood passing through the mitral valve? Certainly there are no definite anatomic landmarks marking this column, which is why equations 7, 8 and 9 are only approximations and \( M, R_c \) and \( R_v \) must ultimately be determined empirically. For \( R_c \), we have seen that \( A \) is the effective valve area, \( c,MVA \). The inertial term \( M \) is largely determined by \( l \), the effective length of the column of blood being accelerated through the mitral valve. Although there is no clear demarcation between the "stagnant" blood in the left atrium and the accelerating blood in the mitral valve, we take the length of the mitral leaflets, about 2 cm, as a first estimate for \( l \), with greater accuracy awaiting empiric measurements. Similarly for \( R_v \), \( l \) is the length over which the blood is subject to the retarding viscous forces of the mitral apparatus. \( R_v \) is associated with the coefficient of discharge, relating the ideal pressure drop across a valve (assuming only Bernoulli pressure conversion) to the observed pressure drop that includes viscous forces (17). This first estimate for \( l \) of 2 cm certainly will need to be modified for severely stenotic valves where subvalvular thickening causes a more prolonged drag on the blood.

This analysis provides support for why viscous effects are much smaller than convective ones in orifice flow. Note that with these estimates for \( A \) and \( l \) as shown, \( R_c \) is 4 times as large as \( R_c \). However, \( R_c \) enters into equation 1 as \( R_c q \), whereas \( R_c \) enters as \( R_c q^2 \). For \( q = 200 \) cm/s, \( R_c q^2 \) will be 50 times larger than \( R_c q \), and therefore viscosity is largely negligible.

**Compliance Modeling**

We thus far have given physical meaning to all of the elements in equation 1. We must now specify the form of the compliance terms in equations 2 and 3. These are derived from the atrial and ventricular pressure-volume curves: compliance is \( dV/dp \) and is the reciprocal of instantaneous chamber stiffness, \( dp/dV \). Although the pressure-volume curves for use in equations 2 and 3 might be simply numeric (that is, a list of volumes with associated pressures), it is preferable to specify them as formulas with just a few variables relating pressure to volume.

**Sample pressure-volume curves.** Several pressure-volume relations suggest themselves to model atrial and ventricular compliance. The simplest such relation is linear: \( p = \alpha V \), where \( V \) is chamber volume and \( \alpha \) is a constant defining chamber stiffness (Fig. 2A). Compliance (\( dV/dp \)) is therefore constant at \( 1/\alpha \).

A more realistic expression for compliance is derived from an exponential pressure-volume relation: \( p = p_0 e^{\alpha V} \), where \( p_0 \) is the pressure in the chamber at 0 volume (Fig. 2B). Chamber stiffness (\( dp/dV \)) is thus \( p_0 \alpha e^{\alpha V} \) or \( \alpha \). Compliance, the reciprocal of stiffness, is therefore \( 1/(\alpha \alpha) \). Such an exponential pressure-volume curve has recently been reported for the canine left atrium/pulmonary venous system (18).

To model active left ventricular relaxation, we must introduce a term to the pressure-volume relation so that pressure displays exponential decay with volume held constant, corresponding to the isovolumic relaxation constant, \( T \) (19): \( p = p_0 (1 + \Gamma e^{-\Gamma / T}) e^{\alpha V} \) (Fig. 2C and 2D). In this equation, \( \Gamma \) represents the ratio of pressure at the time of atrioventricular crossover to the pressure when the ventricle is fully relaxed (with volume being held constant); \( T \) and \( t \) are expressed in milliseconds.

Unfortunately, the simple derivative chain rule used to write equation 3 is no longer valid because pressure is now a function of two independent variables, volume and time, and the effect of changes in each of these variables must be considered in computing \( dp/dt \). By its strict definition, compliance, \( dV/dp \), remains \( 1/(\alpha \alpha) \). However, to determine the rate of change of pressure, one must include both the flow- and time-dependent terms of this pressure-volume relation and so equation 3 is modified:

\[
\frac{dp}{dt} = \frac{\partial p}{\partial V} \frac{dV}{dt} + \frac{\partial p}{\partial t} \frac{dp}{dt} - \frac{q}{C_v} + \frac{\partial p}{\partial t} \frac{dp}{dt}
\]

\[
= \alpha \frac{dV}{dp} - p_0 \alpha V \Gamma e^{-\Gamma / T} / T.
\]

*Partial derivatives must now be used rather than the ordinary derivative \( dV/dp \) because \( V \) is a function of more variables than just \( p \).*
Thus, in early diastole, left ventricular pressure continues to decrease despite positive flow into the chamber, consistent with active relaxation.

**Computer Simulation**

To obtain numeric solutions to this mathematical model, we have programmed equations 1, 2 and 3 on a microcomputer using the C programming language and solving them by fourth-order Runge-Kutta integration (20). One enters the variables of mitral impedance ($R_a$, $R_e$ and $M$) and specifies the form and variables for left atrial and left ventricular compliance, along with the initial chamber pressures, $p_a(0)$ and $p_v(0)$; $q(0)$ is assumed to be 0.

The differential equations are then integrated at 1 ms intervals until the atrial and ventricular pressure gradients equilibrate and the mitral flow is 0. From the computed pressure and flow data are calculated peak transmitral flow rate, peak filling velocity, acceleration time, maximal transmitral gradient, mitral pressure half-time, time to pressure equalization and others. Figure 3 shows a sample prediction of pressure and flow from this system of equations for a simulated situation of mitral stenosis. For this simulation, $R_a = 1.0$, $R_e = 4$, and $M = 3$ ($A = 0.7 \text{ cm}^2$, $L = 2 \text{ cm}$). Atrial compliance is modeled by an exponential pressure-volume relation; ventricular compliance includes the time-dependent term to model active relaxation, here with $T = 30 \text{ ms}$. $p_v(0) = p_a(0) = 20 \text{ mm Hg}$. By altering the available model variables, we are able to generate predicted pressure and flow curves for almost any clinical situation.

**Simplifications Used to Allow Analytic Solution of the Model**

As useful as a computer simulation may be, more insight can often be gained if one can obtain an analytic solution (that is, a formula that may be written out rather than just be a numeric or graphic solution) to the differential equations under concern. It is frequently valuable to make reasonable simplifications to the governing equations or to consider special cases if the equations can be configured in such a way to be solvable analytically.
Figure 3. Numeric solution to equations 1, 2 and 3 here for a simulated situation of mitral stenosis. Input variables are as shown (see Table 1 for symbols) with the pressure-volume curves corresponding to a left atrial (LA) compliance of 50p and a left ventricular (LV) compliance of 60p with an isovolumic relaxation constant of T = 30 ms. The output values shown are calculated from the computed mitral valve (MV) flow and pressure curves and correspond to clinically observable variables.

For instance, it has been noted that viscous effects are negligible in stenotic valve flow, and so we may reasonably set Rₐ to 0 in equation 4. Additionally, the effect of the inertial term in equation 4 is to cause changes in flow to lag a few milliseconds behind changes in pressure, which may be unimportant for many situations. If M is set to zero, it forces the numerator on the right side of equation 4 to be zero, or Δp = Rₐq², and substituting for Rₐ: Δp = ρq²/2(cₐ MVA)². This final equation can be converted to the Gorlin equation by solving for MVA rather than Δp: MVA = qνp/(cₐ = p) = q/50.4 cₐνΔp).

Now consider the special case where Cₐ and Cᵥ (and thus Cₐ) are constant rather than varying with pressure or time. This particular simplification is applicable to the initial observations with the in vitro model. We rewrite equation 5 as q = -Cₐ(dΔp/dt). Substituting this expression for q in the previous equation and rearranging to solve for dΔp/dt yields

\[ d\Delta p/dt = -cₐ MVA \sqrt{2\Delta p}/Cₐ, \]  

which is solvable analytically. For an initial pressure gradient, Δp₀, it has the solution \( \Delta p(t) = (\sqrt{\Delta p₀} - (2cₐ MVA/Cₐ)t)^2 \). (11)

Solving equation 11 for t when \( \Delta p = \Delta p₂/2 \), we obtain an analytic expression for mitral pressure halftime (in milliseconds):

\[ T₁/₂ = 11.6Cₐ \sqrt{\Delta p₀/(cₐ MVA)}. \]  

Equation 11 was used as the predicted pressure decay curve in the in vitro model (see later). Equation 12 states that the mitral pressure half-time is inversely proportional to mitral valve area (as it is commonly used clinically) but also directly proportional to mean net left atrial and ventricular compliance and the square root of the initial transmitral gradient; it has been discussed in greater detail in previous reports (11,12).

Methods

In Vitro Verification

As initial verification of the pressure and flow predictions of the mathematic model, an in vitro analog of the left atrium...
and ventricle has been built (Fig. 4). Rather than simply mimic transmural flow by a mechanical pump, this in vitro model has been designed to mimic the forces responsible for generating mitral valve flow. In addition, many of the variables needed to solve equations 1, 2 and 3 ($C_n$, $C_v$, $p_0(0)$, $p_t(0)$, MVA) may be independently adjusted and accurately measured. The observed pressure and flow curves may then be compared with those predicted by computer to assess the adequacy of our mathematic formulation.

**Description of the model.** The in vitro model consists of a Plexiglas chamber about 6 cm (W) x 14 cm (L) x 57 cm (H) in size with a vertical septum to divide it into a proximal “left atrial” side (6 x 6 x 57 cm) and a distal “left ventricular” side (6 x 8 x 57 cm). At the bottom of the septum is a mount for the mitral valve orifice, through which blood flows from the atrial to the ventricular side by gravity. The septal mount has been designed to hold a wide variety of orifices including prosthetic and native mitral valves, but for this study it held round orifices in thin plastic sheeting from 0.3 to 3.0 cm² in area. Fluid-filled pressure transducers are connected to the proximal and distal chambers by short, rigid tubes. These ports are 3 cm lateral to and 2 cm proximal and distal to the center point of the orifice. Transmural flow is measured by a 24 mm electromagnetic flow probe (Spectramed) mounted around the orifice. The ventricular chamber is sealed airtight at the top and connected to a solenoid valve, which can be opened on computer command. A hand pump is used to raise the pressure in the ventricular side to force blood over to the atrial side, where it remains until the solenoid valve is opened, releasing pressure in the ventricular chamber. Compliance in each chamber is taken as the volume of blood necessary to raise the pressure at the transducer by 1 mm Hg and is proportional to the cross-sectional area of the chamber. Compliance is lowered in each chamber by inserting vertical Plexiglas plates (6 x 1 x 57 cm) into the chamber to displace a known amount of blood.

**Data acquisition.** Atrial and ventricular pressures and orifice flow were preamplified by a Hewlett Packard 7700 multichannel recorder and digitized at 25 to 200 Hz by a Data Translation DT-2801 A/D board interfaced with a microcomputer. All data acquisition and on-line analysis was performed with customized software written for the Asyst scientific system (Macmillan Software Company). On user command, acquisition of pressure and flow data was initiated; 100 ms later, the solenoid valve opened to return the air pressure in the ventricular chamber to ambient, establishing a pressure gradient between the two chambers, and causing the excess blood in the atrial chamber to flow through the orifice by gravity. Pressure and flow were digitized until pressures had equilibrated. These data were smoothed with a moving 10-point Blackman filter and stored for further analysis (21).

**Experimental Protocol**

For initial in vitro validation of the mathematic predictions, we used eight round orifices (in plastic sheeting) ranging from mitral valve area (MVA) = 0.3 to 3.0 cm². Net compliance was varied from 29 down to 16 cm³/mm Hg by inserting up to three vertical plates into the left atrial chamber. Heparinized canine blood was used for all experiments. Blood was pumped to the left atrial side to establish an initial gradient ($\Delta p_0$) between 1 and 14 mm Hg. Left ventricular pressure was subtracted from left atrial pressure, yielding $\Delta p(t)$, and data were collected beginning with valve opening and ending with pressure equalization. This observed pressure decay curve was then fitted by Marquardt nonlinear least squares approximation to the specific parabolic form predicted by equation 11, $p(t) = (A_0 - A_10)^2$. Analysis of variance and linear correlation was used to test the agreement of this predicted form to the observed $\Delta p(t)$. Equation 11 was judged to be the appropriate governing equation if this constrained parabolic form fit the observed pressure decay curve with $r > 0.99$; if no significant further improvement could be obtained using an unconstrained second-order polynomial curve (which includes ($A_0 - A_10^2$) as a subset); and if the value of the fitted variables, $A_0$ and $A_1$, could be predicted from the known model variables: $A_0 = V \Delta p_0$ and $A_1 = 25.2c_0^- MVA/C_n$. The latter identity includes the coefficient of orifice contraction, generally between 0.6 and 0.9 for orifices of this type. We, therefore, used this expression to refine the value of $c_0$ and judge its variation with orifice area and compliance. Correlation coefficients were compared after first performing Fisher’s $z$-transformation.

**Results**

Figure 5 demonstrates a typical set of pressure curves from the in vitro model, here for a valve area of 2.0 cm², atrial compliance of 21.7 cm³/mm Hg and left ventricular compliance of 66.5 cm³/mm Hg (net compliance of 16.3 cm³/mm Hg) and initial pressure gradient of 12.1 mm Hg. The constrained parabola predicted by equation 11 fitted to this
Pressure Decay Constant (\(\sqrt{\text{mmHg/sec}}\))

![Graph showing pressure decay constant against orifice area](image)

Figure 6. Ability of equation 11 to predict rate of pressure decay in the in vitro model. Shown on the y axis are pressure decay variables (that is, \(A,\) in \([A_0 - A_1 t]^2\)) plotted against orifice area for two different levels of net chamber compliance. Excellent correlation was seen with 25.2c,MVA/C,,

curve is shown with excellent correlation (\(r = 0.9986\)). The unconstrained quadratic form yielded no significant improvement in fit despite the additional degree of freedom.

For 16 different combinations of MVA, \(\Delta p_0,\) and \(C_p,\) mean correlation of the constrained curve fitted to the data averaged \(r = 0.9982.\) The general second-order fit yielded only minor improvement with \(r = 0.9987.\) Because of the additional degree of freedom, the F-value for the general fit was lower than that for the constrained fit (70704 versus 94481, \(p = 0.05).\)

Ability of parameters to predict pressure decay. Figure 6 shows the pressure decay coefficient (\(A,\) in the constrained parabola \([A_0 - A_1 t]^2\)) plotted against orifice area for two levels of compliance. Observed values of \(A,\) were compared with the predicted value (25.2c,MVA/C,,

Figure 7. Ability of equation 11 to predict initial pressure gradient in the in vitro model (\(A_0^2\) in \([A_0 - A_1 T]^2\)).

Discussion

Relation of Current Results to the Mathematic Model of Mitral Flow

The results of this in vitro testing have shown excellent agreement with the predictions of our mathematic model of mitral flow for a very specific situation: where 1) atrial and ventricular compliance (and thus net compliance) are constant; and 2) the orifice is such that the effects of viscous resistance and inertial mass are so small that convective resistance is the only component of mitral impedance. Despite these specifications, this subset of our mitral flow model has proved useful in examining the mitral pressure half-time (11,12), demonstrating significant influence of chamber compliance and initial pressure gradient on this index of mitral valve area.

In the more general clinical situation, in which mitral flow is analyzed to evaluate left ventricular diastolic performance, it is critical that our modeling of left ventricular compliance allow for variation with pressure (for example, an exponential pressure-volume relation) and time (for active relaxation). With this additional complexity, equations 1 and 3 will generally no longer be solvable analytically, only numerically by computer. It would be very helpful if our in vitro model could be modified to simulate time and pressure variation in compliance and so generate pressure decay data to compare with these numeric predictions.

Enhancements to the in Vitro Model

Modeling variable compliance in the in vitro model. Note that compliance is constant in the Plexiglas model because the cross-sectional area of each chamber is independent of height above the mitral orifice (that is, the chambers are rectangular). If, instead, the area of the chamber varied with height above the orifice, then so would compliance. For the typical situation of increasing chamber stiffness with increasing pressure, the chamber would need to become narrower at higher points above the orifice.

Thus far we have lowered chamber compliance by inserting rectangular plates to displace fluid. If instead we insert wedges, curved or triangular, we will vary the cross-sectional area (and hence compliance) at each level of chamber pressure. For example, Figure 8 shows a schematic side view of the left atrial chamber from the in vitro model with the corresponding constant pressure-compliance and

with decreasing valve size, perhaps reflecting increased viscous resistance of the smallest orifices.
Figure 8. Schematic side view of in vitro chamber (A) with corresponding compliance (B) and pressure-volume (C) curves (assuming that this chamber has a width into the page of 1 cm). Because the chamber is rectangular, compliance is constant and pressure is a linear function of volume.

linear pressure-volume curves beside it. In contrast, Figure 9 is an example of a triangular wedge inserted into the chamber with its corresponding curves displaying a dramatic change in the chamber pressure-volume relation. Finally, Figure 10 shows a curved wedge that reduces the cross-sectional area of the chamber, inversely proportional to the height above the orifice. This compliance relation is thus similar to the $l/t$ relation described in Fig. 2B and (as Figure 10C shows) corresponds to an exponential pressure-volume curve. By a judicious shaping of these wedges, one should be able to model most pressure-compliance relations.

Modeling active relaxation in the in vitro model. Recall that the Plexiglas model is prepared for data acquisition by pumping air into the left ventricular side (which is sealed) raising the pressure and forcing blood onto the left atrial side. On computer command, a valve is opened and the excess air pressure in the ventricular chamber is released through a 2 cm diameter tube that is 50 cm long. Pressure release occurs within 10 ms (before any appreciable blood flow has occurred through the mitral orifice) and thus the full prerelease height difference between the atrial and ventricular chambers is available to establish the maximal early diastolic AV pressure gradient ($\Delta p_o$). This is analogous to in vivo left ventricular relaxation with a relaxation constant ($T$) of only 2 or 3 ms (the normal value being 25 to 35 ms). If instead the excess air in the ventricular chamber were released through a smaller, restrictive orifice, then the establishment of the transorifice pressure gradient would be delayed, which is more consistent with the known in vivo situation.

One may calculate the approximate area of the release valve needed to depressurize the ventricular chamber with a "T" of 30 ms by applying equation 12 for the pressure half-time, but correcting for the different density of air (0.0012 g/cm$^3$ at 20°C) and using the correct compliance.* The volume of air above the blood in the ventricular cavity is approximately 2,300 cm$^3$. It takes about 3 cm$^3$ of additional air to raise the pressure in the chamber by 1 mm Hg (2,300/760) so net left atrial and ventricular compliance ($C_n$) is about 3 cm$^3$/mm Hg. Rewriting equation 12 with these values gives:

$$T'_{1/2} = (11.63\sqrt[3]{\Delta p_o/A}) \times \sqrt{0.0012} = \sqrt[3]{\Delta p_o/A}.$$  

Thus a $T'_{1/2}$ of 30 ms could be achieved with a $\Delta p_o$ of 4 mm Hg by discharging the left ventricular chamber through an orifice approximately 0.015 cm$^2$ in area. Although delaying left ventricular "relaxation" in this manner is not entirely analogous to the in vivo situation, it should be close enough to allow testing of some of the predictions of the mathematic model.

*This assumes only convective losses causing pressure drop. In fact, it can be shown that viscous effects are about a factor of 100 less than this and so may rightly be neglected.
Alternative Mathematic Formulations of Mitral Flow

Navier-Stokes equation. Different mathematic approaches to modeling mitral valve flow have been proposed. The most complete model would require the numeric solution of the Navier-Stokes equations for incompressible flow, four coupled partial differential equations with complex superimposed boundary conditions (that is, the wall of the atrium and ventricle). In this approach blood flow is described at every point in the atrium and ventricle by a velocity vector, \( \vec{\mathbf{v}} \) (in essence three components of velocity, \( v_x, v_y, \) and \( v_z \)) and a pressure scalar, \( p \); \( \vec{\mathbf{v}} \) and \( p \) are each functions of position (\( x-, y-, \) and \( z- \)coordinate within the cardiac chambers) and time (\( t \)). At every point in the atrium and ventricle and at each point in time, the following differential equations must hold (22):

\[
\nabla \cdot \vec{\mathbf{v}} = 0 \\
\frac{D\vec{\mathbf{v}}}{Dt} = -\nabla p + \vec{\mathbf{F}} + \eta \nabla^2 \vec{\mathbf{v}},
\]

where \( \vec{\mathbf{F}} \) is a body force (such as gravity) acting on the fluid and \( D/Dt \) is the “material” derivative for moving fluid, a vector operator which for the \( x- \)component of velocity (in cartesian coordinates) is

\[
\frac{\partial \vec{\mathbf{v}}}{\partial t} + v_x \frac{\partial \vec{\mathbf{v}}}{\partial x} + v_y \frac{\partial \vec{\mathbf{v}}}{\partial y} + v_z \frac{\partial \vec{\mathbf{v}}}{\partial z}.
\]

\( \nabla \) and \( \nabla^2 \) are defined in Table 1.

The first of the Navier-Stokes equations is simply a differential version of the continuity equation, stating that, because blood is incompressible, the amount of fluid coming into a region must be balanced by the amount leaving that region. The second equation is actually three equations (because it must hold identically for the three components of velocity) and represents the effect of pressure gradients and viscosity on local blood flow. These two equations appear deceptively simple and in fact are prohibitively expensive to solve even on the largest supercomputers. Simple arithmetic will show why: achieving 1 mm spatial resolution to the solution requires that 1,000 points per cm\(^2\) be evaluated, or >100,000 points for the entire left heart. To then achieve 1 ms temporal resolution implies that we must solve for three velocity components and pressure at approximately 100,000,000 spatiotemporal points all interconnected in a complex four-dimensional mesh. Advancing forward 1 ms in time requires the simultaneous solution of ~400,000 linear equations, a truly prodigious task. Factoring in the position and material properties of the boundaries only adds to the complexity.

The mitral flow model that comes closest to this full spatiotemporal solution is that developed by Peskin (working in collaboration with Yellin, McQueen, and others) (23–25). Even this quite sophisticated approach significantly simplifies the Navier-Stokes equations by precluding turbulence and by solving only a two-dimensional approximation to the left heart, not a full three-dimensional model. Despite these simplifications Peskin’s approach has proved useful in the design of hydrodynamically optimal prosthetic mitral valve (26–28).
Spatial resolution may be unnecessary. In large part, however, the degree of spatial resolution provided by solving the Navier-Stokes equations is wasted given the limits of resolution with which we can measure pressure and flow within the heart. Certainly pressure is nearly always measured as a single quantity for the left atrium and another for the left ventricle, not as a continuous function that may vary slightly within each chamber. Similarly, flow measurements to assess atrioventricular interaction and mitral impedance are generally taken at the point of maximal velocity within the mitral apparatus (usually the tips of the mitral leaflets). Knowing the pressure and velocity vector at the far reaches of the left atrium is rarely of great interest, but these points are evaluated by the Navier-Stokes approach along with the generally more interesting points in the principal mitral valve flow. One situation in which three-dimensional modeling is necessary is in the analysis of color-coded Doppler signals, which do provide information throughout the heart on one component of the blood velocity vector. This may explain why quantitative analysis of color-flow Doppler has proved so difficult.

Advantages of lumped variable modeling. The mathematical model described in this review offers several computation savings when compared with the Navier-Stokes equations. The general approach we have used is termed lumped variable modeling, because it lumped together spatially distributed quantities (such as the pressure throughout the left atrium) into a single scalar quantity (“left atrial pressure”). The numeric economy obtained by converting 100,000 pressures and velocity vectors into a single variable is obvious. Furthermore, because spatial gradation has been eliminated by this lumping, so too have all spatial derivatives. The only derivatives to remain are those with respect to time and these are ordinary derivatives, not partial ones. Solving systems of ordinary differential equations numerically is much more straightforward than solving partial differential equations. The computational savings of the lumped variable approach is so great that these equations may be readily solved on a microcomputer.

Other lumped variable models. Meisner, working in Yellin’s group (29), recently described a lumped variable model similar in many ways to our own. It has been used to predict the effect of the timing of atrial systole on ventricular filling (30) and to analyze the interaction of atrial preload and pulmonary venous inflow on transmitral flow (31,32).

Kovacs et al. (33) have also developed a lumped variable model of left ventricular filling, describing mitral flow as an over-damped harmonic oscillator, resulting in a linear second-order differential equation. Active relaxation is modeled as a displacement of a mass on a spring with ventricular “suction” resulting when the mass is released. Because of a desire to keep the governing equation linear, mitral resistance is modeled as proportional to flow (that is, all viscous resistance, no convective), whereas the results of our in vitro testing demonstrate that the overwhelming component of mitral impedance is proportional to the “square of the flow rate.” Additionally, atrial and ventricular pressures do not enter directly into this model and must be estimated by indirect means. This, however, might be beneficial if useful data concerning ventricular relaxation and compliance could...
Table 1. Mathematic Symbols

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>$a$</td>
<td>Acceleration of blood through mitral valve (cm$^2$ s$^{-2}$)</td>
</tr>
<tr>
<td>$A$</td>
<td>Cross-sectional area of blood column passing through the mitral valve: effective area of the mitral valve (cm$^2$)</td>
</tr>
<tr>
<td>$A_p$, $A_t$, $A_s$</td>
<td>Variables used in fitting observed data to predicted equations</td>
</tr>
<tr>
<td>$\vec{B}$</td>
<td>Body force vector (such as gravity) acting on fluid</td>
</tr>
<tr>
<td>$c_x$</td>
<td>Coefficient of orifice contraction (dimensionless)</td>
</tr>
<tr>
<td>$C_{p(t)}$</td>
<td>Left atrial (pulmonary vein) compliance (cm$^2$/mm Hg)</td>
</tr>
<tr>
<td>$C_s$</td>
<td>Net left atrial and ventricular compliance: $C_{p(t)} + C_{p(t)}$</td>
</tr>
<tr>
<td>$C_{p(t)}$</td>
<td>Left ventricular compliance (cm$^2$/mm Hg)</td>
</tr>
<tr>
<td>$e$</td>
<td>Euler's constant 2.71828</td>
</tr>
<tr>
<td>$F$</td>
<td>Force driving blood through mitral valve</td>
</tr>
<tr>
<td>$f$</td>
<td>Length of blood column passing through mitral valve</td>
</tr>
<tr>
<td>$m$</td>
<td>Mass of blood flowing through mitral valve</td>
</tr>
<tr>
<td>$M$</td>
<td>Inertial impedance of mitral valve (g-cm$^{-4}$)</td>
</tr>
<tr>
<td>$MVA$</td>
<td>Anatomic mitral valve area (cm$^2$)</td>
</tr>
<tr>
<td>$p$</td>
<td>Pressure (mm Hg or dyne-cm$^{-2}$)</td>
</tr>
<tr>
<td>$p_L(t)$</td>
<td>Left atrial pressure (mm Hg)</td>
</tr>
<tr>
<td>$p_V(t)$</td>
<td>Left ventricular pressure (mm Hg)</td>
</tr>
<tr>
<td>$q$</td>
<td>Flow rate through mitral valve (cm$^3$/s)</td>
</tr>
<tr>
<td>$R_{a}$</td>
<td>Convective resistance of mitral valve (g-cm$^{-4}$)</td>
</tr>
<tr>
<td>$R_{x}$</td>
<td>Viscous resistance of mitral valve (g-cm$^{-2}$s$^{-1}$)</td>
</tr>
<tr>
<td>$t$</td>
<td>Time (s or ms)</td>
</tr>
<tr>
<td>$T$</td>
<td>Isovolumic relaxation time constant (ms)</td>
</tr>
<tr>
<td>$\nu$</td>
<td>Velocity of blood passing through mitral valve (cm/s)</td>
</tr>
<tr>
<td>$\nu_0$</td>
<td>Velocity vector of blood, a function of position in heart</td>
</tr>
<tr>
<td>$V_L$</td>
<td>Left atrial (pulmonary vein) volume (cm$^3$)</td>
</tr>
<tr>
<td>$V_V$</td>
<td>Left ventricular volume (cm$^3$)</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>Chamber stiffness variable (mm Hg-cm$^{-3}$) for linear pressure-volume curve, cm$^{-3}$ for exponential curve</td>
</tr>
<tr>
<td>$\gamma$</td>
<td>Effect of active relaxation on left ventricular pressure-volume curve, that is, the ratio of pressure at time of mitral valve opening to pressure if ventricle were fully relaxed at the same volume (dimensionless)</td>
</tr>
<tr>
<td>$\eta$</td>
<td>Viscosity, 0.03 poise for blood (g-cm$^{-1}$s$^{-1}$)</td>
</tr>
<tr>
<td>$\rho$</td>
<td>Density, 1.05 g/cm$^3$ for blood; 0.0012 g/cm$^3$ for air (25°C)</td>
</tr>
<tr>
<td>$\nabla$</td>
<td>Gradient operator, $\partial$/$\partial x$ + $\partial$/$\partial y$ + $\partial$/$\partial z$</td>
</tr>
<tr>
<td>$\nabla^2$</td>
<td>Laplacian operator, $\partial^2$/$\partial x^2$ + $\partial^2$/$\partial y^2$ + $\partial^2$/$\partial z^2$</td>
</tr>
</tbody>
</table>

2) The mitral impedance variables ($M$, $R_a$, and $R_x$) have no definite a priori association with mitral morphology. We have derived reasonable approximations to these, but further refinement awaits experimental study. It may be, however, that these hydrodynamic variables tell more about valvular function than their morphologic correlates (for example, the effective valve area means more than the anatomic area).

3) Equations 1, 2 and 3 currently proceed from impedance and compliance data to yield pressure and flow predictions. It would be more clinically useful to invert this process, using observed pressure and flow data to obtain estimates of chamber compliance and valve impedance.

Conclusions

We have described a mathematic formulation for mitral valve flow that uses measures of mitral valve impedance and left atrial and ventricular compliance to predict the time course of diastolic mitral flow and atrial and ventricular pressure. From these computed curves, we may then calculate many of the Doppler and hemodynamic indexes used clinically in evaluating mitral valve disease and left ventricular diastolic function. The fundamental validity of this mathematic approach has been verified in an in vitro model of the left heart, with constant left atrial and ventricular compliance. This theoretic approach allows us to conceptualize the forces responsible for transmitial blood flow. It may also help unify the Doppler and catheterization assessments of mitral valve disease and disorders of left ventricular filling.

References

FLUID DYNAMICS MODEL OF MITRAL FLOW


