Inaccuracy of Mitral Pressure Half-Time Immediately After Percutaneous Mitral Valvotomy

Dependence on Transmitral Gradient and Left Atrial and Ventricular Compliance

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Mitral pressure half-time (T1/2) is widely used as an independent measure of mitral valve area in patients undergoing percutaneous mitral valvotomy. However, fluid dynamics theory predicts T1/2 to be strongly dependent on chamber compliance and the peak transmitral gradient, which are variables that change dramatically with valvotomy. These theoretical predictions were tested in an in vitro model of the left heart where valve area, chamber compliance, and initial gradient were independently adjusted. Measured T1/2 was observed to vary inversely with orifice area and directly with net chamber compliance and the square root of the initial pressure gradient. Theoretical predictions of T1/2 agreed with observed values with r=0.998. To test this theory in vivo, the hemodynamic tracings of 18 patients undergoing mitral valvotomy were reviewed. Predictions were made for T1/2 assuming dependence only on valve area; these showed some correlations before valvotomy (r=0.48–0.64, p<0.05) but none after valvotomy (r=0.05–0.28, p=NS). Predictions for T1/2 based on the theoretical derivation (and thus including compliance and pressure in their calculation) were much better: before valvotomy, r=0.93–0.96, p<0.0001; after valvotomy, r=0.52–0.66, p<0.05. These data indicate that T1/2 is not an independent inverse measure of mitral valve area but is also directly proportional to net chamber compliance and the square root of the initial transmitral gradient. These other factors render T1/2 an unreliable measure of mitral valve area in the setting of acute mitral valvotomy. (Circulation 1988;78:980–993)

Almost 4 decades after Gorlin and Gorlin1 first presented their hydrodynamic formulation for estimating mitral valve area (MVA), the accurate assessment of mitral stenosis remains controversial.2–4 With the advent of percutaneous mitral valvotomy, the number of patients undergoing valve dilation as opposed to replacement will undoubtedly increase, and accurate MVA measurement will become even more important as the short- and long-term results of valvotomy are assessed. Although the Gorlin equation remains the principle invasive measure of the success of valvotomy, the need for serial follow-up demands a reliable noninvasive assessment of MVA. In current clinical practice, this is typically either echocardiographic planimetry of the mitral orifice or the mitral pressure half-time (T1/2) derived from Doppler data.5,6 T1/2 has recently been suggested to be more accurate than planimetry in patients after surgical commissurotomy.7 Despite its widespread use in patients undergoing balloon valvotomy, however, the accuracy of T1/2 has not been critically tested in this clinical setting.

T1/2 (the time required for the left atrioventricular pressure gradient to fall to half of its maximal early diastolic value) was originally developed with cathe-
terization data and then applied by Hatle and colleagues to the emerging field of Doppler echocardiography, where it has rapidly gained acceptance as an accurate estimate of MVA in both native and prosthetic valves. Central to its usefulness is the belief that the T\textsubscript{1/2} varies inversely with MVA, and is relatively unaffected by changes in other hemodynamic variables such as heart rate, cardiac output, left atrial (LA) or ventricular (LV) pressure, and the severity of mitral regurgitation.

We have recently described a theoretical derivation for T\textsubscript{1/2} based on fluid dynamics principles. In this formulation, T\textsubscript{1/2} is predicted to vary inversely with MVA (as observed empirically) but also to vary directly with net LA and LV compliance and the square root of the initial pressure gradient. Thus, in clinical situations where compliance or pressure gradient is changing significantly, theory would predict T\textsubscript{1/2} to be inaccurate. In particular, because pressure gradient is known to fall dramatically with valvotomy, T\textsubscript{1/2} may be an inaccurate measure of MVA in this clinical situation. The predictions of this mathematical model, however, have yet to be validated, and the effects of other variables, such as viscosity and variation in the coefficient of orifice contraction, are unclear.

Thus, the first purpose of this study was to test the validity of our theoretical formulation of T\textsubscript{1/2} in an in vitro model of mitral flow where orifice area, chamber compliance, and driving pressure could be independently adjusted. The second broad goal was to assess the accuracy of the traditional use of T\textsubscript{1/2} to determine MVA in patients undergoing percutaneous mitral valvotomy and to compare these results with those obtained with our theoretical formulation, which includes compliance and pressure effects.

Patients and Methods

Theoretical Background

Empirical formulation for mitral pressure half-time. In their ground breaking work on Doppler echocardiography, Hatle and colleagues provided an empirical formula relating T\textsubscript{1/2} to anatomic MVA: MVA = 220/T\textsubscript{1/2}, which was validated in 20 patients with mitral stenosis undergoing catheterization. This has remained essentially unchallenged in the Doppler assessment of MVA. In this article, we compare competing predictions for T\textsubscript{1/2} rather than MVA, and therefore, we have inverted this equation:

\[ T_{1/2} = \frac{220}{MVA} \] (1)

Equation 1 is used throughout this article as the traditional or empirical standard against which to compare the observed T\textsubscript{1/2} in the patients undergoing valvotomy as well as the theoretical predictions described below.

Fluid dynamics model of mitral valve flow. We have previously described a lumped variable mathematical model for mitral valve flow based on Newton’s second law of motion and the definition of chamber compliance (all mathematical symbols are defined in Table of Abbreviations). In this model, the left atrium and pulmonary veins are assumed to be a common chamber receiving the full cardiac stroke volume in systole and discharging it by elastic recoil through the mitral valve into the LV during diastole. Both the LA and LV chambers are described by terms relating instantaneous compliance (dV/dp) to chamber pressure; LV compliance (C\textsubscript{v}) may also be a function of time to account for active LV relaxation. In its most general formulation, the governing equations for LA and LV pressure (p\textsubscript{a} and p\textsubscript{v}) and MV flow (q) are three coupled nonlinear differential equations:

\[ \frac{dq}{dt} = (p_a - p_v - R_c q^2 - R_d q)/M \] (2)
\[ \frac{dp_a}{dt} = -q/C_a \] (3)
\[ \frac{dp_v}{dt} = q/C_v \] (4)

Mitral valve impedance is described by three factors: 1) convective resistance (R\textsubscript{c}) reflecting the conversion of pressure energy to kinetic energy as blood accelerates through the valve, 2) viscous resistance (R\textsubscript{d}) reflecting pressure drop due to viscosity of flow, and 3) an inertial term (M) representing the mass of blood flowing through the valve that causes flow changes to lag a few milliseconds behind pressure changes.

Theoretical derivation for mitral pressure half-time. In their general form, Equations 2, 3, and 4 are solvable only by computer. It is useful, therefore, to introduce reasonable simplifications spe-
specific to the clinical situation of mitral stenosis in hopes of obtaining equations that may be solved by analytical means. The first simplification is to set viscous mitral resistance ($R_v$) to zero as is done in the Gorlin formulation of MVA and as is implicitly done in the T1/2 formulation by its use of the Bernoulli equation to relate velocity to pressure gradient. This seems reasonable because convective resistance ($R_c$) contributes to pressure drop in proportion to flow squared, whereas viscous resistance contributes only in direct proportion to flow. Thus, at all but the lowest flows, convective resistance should predominate. This assumption of negligible viscous effects was tested empirically in the in vitro model, vide infra. The second simplification is to set the inertial term (M) to zero; this simply forces flow to follow the pressure gradient instantaneously rather than to be delayed by a few milliseconds. Because flow in mitral stenosis typically is of the order of several hundred milliseconds, this assumption seems quite reasonable. Finally, we consider LA and LV compliance to be the mean chamber compliances throughout diastole rather than allowing them to vary instantaneously. This is reasonable because our purpose in solving these equations is to yield an expression for T1/2, a quantity that reflects mean LA, mitral valve, and LV properties during an extended period of diastole, not instantaneous changes. Furthermore, we will show that it is possible to use mean compliance data from a wide range of pressures to derive semiquantitative expressions relating instantaneous compliance to pressure and then to integrate these expressions to yield approximate pressure-volume relations for the atrium and the ventricle.

We next introduce notational simplifications: pressure gradient ($\Delta p$) defined as $p_s - p_l$ and mean net compliance ($C_n$) defined for two chambers in series as $(1/C_s + 1/C_o)^{-1}$ or $C_n = (C_s + C_o)$. Note that net chamber compliance is always less than either LA or LV compliance. With these simplifications, Equation 2 becomes

$$\Delta p = R_c q^2$$  \hspace{1cm} (5)

Subtracting Equation 4 from Equation 3 yields

$$d\Delta p/dt = -q/C_n$$  \hspace{1cm} (6)

Equation 5 is nothing more than the simplified Bernoulli equation ($\Delta p = \frac{1}{2} \rho v^2$) with $R_c = \rho/2(c,C_{MVA})^2$, that is, $\Delta p = \rho q^2/2(c,MVA)$, where MVA is the anatomic mitral valve area, and $c$ is the coefficient of orifice contraction, the ratio of effective to anatomic orifice area. Solving for q in this expression and substituting into Equation 6 yields

$$d\Delta p/dt = -c(MVA)\sqrt{2\Delta p/\rho/C_n}.$$  \hspace{1cm} (7)

This may be integrated directly from initial pressure gradient, $\Delta p_0$: $\Delta p(t) = \left[\sqrt{\Delta p_0 - [c(MVA)/(C_n\sqrt{2\rho})]^2}\right]^2$. By expressing pressure in millimeters of mercury and time in seconds, this becomes

$$\Delta p(t) = \left[\sqrt{\Delta p_0 - (25.2 c(MVA)/C_n)^2}\right]^2$$  \hspace{1cm} (8)

Solving for t when $\Delta p = \Delta p_u/2$ yields an analytical expression for T1/2:

$$T_{1/2} = 11.6 C_n\sqrt{\Delta p_u/(c,MVA)}$$  \hspace{1cm} (9)

where T1/2 is expressed in milliseconds. Equation 9 is used throughout the article as the theoretical prediction for T1/2 for comparison with observed valvotomy or in vitro data.

**In Vitro Model**

In vitro modeling was undertaken to answer the following questions: 1) what is the relative contribution of viscous and convective resistance to overall mitral impedance; that is, is it reasonable to neglect viscosity in our simplifications? 2) What is the coefficient of contraction across a range of orifice areas? 3) Does Equation 9 accurately describe observed T1/2 for a wide range of chamber compliances, initial pressure gradients, and orifice areas?

**Description of the model.** Figure 1 illustrates the in vitro model used in this study. Rather than mimic mitral-flow profile with a pump, it uses gravity to mimic the dynamic forces at work in causing mitral valve flow. The model consists of a Plexiglas chamber approximately 6 cm (W) x 14 cm (L) x 57 cm (H) in size with a vertical septum to divide it into a “left atrial” side (6 x 6 x 57 cm) and a “left ventricular” side (6 x 8 x 57 cm). At the bottom of the vertical divider is a mount for the mitral valve, which for this study held round orifices from 0.3 to 3.0 cm2 in area. Fluid-filled pressure transducers are connected to the LA and LV chambers at the orifice level by short, wide-bore rigid tubes. The LV chamber is sealed at the top and connected to a solenoid valve that can be opened on computer command.

Heparinized canine blood was used for all experiments. A hand pump was used to increase pressure in the LV side to force blood over to the LA side. Compliance in each chamber was taken as the volume of blood necessary to raise the pressure at the transducer by 1 mm Hg and was proportional to the cross-sectional area of the chamber. Compliance was 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 and decrease the cross-sectional area of the chamber.

**Data acquisition.** LA and LV pressures and orifice flow were preamplified by a Hewlett-Packard 7700 multichannel recorder (Andover, Massachusetts) and digitized at 25–200 Hz by a Data Translation DT-2801A A/D board (Marlboro, Massachusetts) 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, New York, New York). On software command, data acquisition was initiated, and the solenoid valve was opened to return the air pressure above the LV chamber blood to ambient pressure, establishing a pressure gradient...
between LA and LV and causing the excess blood in the LA chamber to flow through the orifice by gravity. Pressure and flow were digitized at 200 time intervals, generally until pressures had equilibrated. These data were smoothed with a moving ten-point Blackman filter and stored for further analysis.

Relative importance of convective versus viscous resistance in valvular stenosis. As explained above, we have neglected viscous resistance in our theoretical formulation of $T_{1/2}$, leaving convective resistance as the only component of mitral impedance. If convective resistance indeed predominates, then the differential equation for pressure gradient will be of the form $d\Delta p/dt \propto -\Delta p$, whose solution is a parabola, $(A_0 - A_1 t)^2$, where $A_0$ and $A_1$ are constants to be fitted to the observed data. Note that Equation 8 is of this form. Accordingly, this predicted form was fitted to the observed in vitro pressure decay curve by varying the variables $A_0$ and $A_1$ with Marquardt's nonlinear least-squares method. Analysis of variance was used to estimate the goodness of this fit to the observed pressure decay. The fit of this constrained parabola was compared with that obtained by a general second-order polynomial $(A_0 t^2 + A_1 t + A_2)$ of which $(A_0 - A_1 t)^2$ is a subset.

On the other hand, if viscous resistance dominated convective, then the governing differential equation would be of the form, $d\Delta p/dt \propto -\Delta p$, whose solution is an exponential decay curve, $A_0 e^{-At}$. This form, therefore, was also fit to the observed pressure curve, and the merit of the parabolic versus the exponential fit (by analysis of variance) was used to establish the relative importance of convective versus viscous resistance, respectively. Correlation coefficients were compared after Z transformation.

Calculation of the coefficient of contraction. Comparing the fitted form $(A_0 - A_1 t)^2$ to Equation 8 establishes the correspondence $A_0 = \sqrt{\Delta p}$ and $A_1 = 25.2c_{MVA}/C_n$.

Because MVA and net chamber compliance were known from the experimental setup, the coefficient of orifice contraction could be calculated for each curve from the fitted decay constant $A_1$. This was averaged for all of the runs to yield an average coefficient of orifice contraction.

Comparison of observed in vitro pressure half-time to theoretical prediction. For each pressure-decay curve, the time required for the pressure gradient to fall to half of its initial value ($T_{1/2}$) was measured. Multiple pressure-decay curves were measured with MVA ranging from 0.3 to 3.0 cm², $\Delta p_0$ from 0.5 to 14 mm Hg, and $C_n$ from 16 to 29 cm²/mm Hg. Linear correlation was calculated for the observed $T_{1/2}$ versus the predicted $T_{1/2}$ based on Equation 9.

Patient Studies

The hemodynamic tracings of 18 patients obtained during percutaneous mitral valvotomy were studied. There were four men and 14 women with a mean age of $54.9 \pm 3.4$ years (mean \pm SEM). All had a clinical diagnosis of mitral stenosis and underwent valvotomy by the transseptal route. Six patients had angiographic mitral regurgitation before valvotomy (five with grade 1, one with grade 2; mean, 0.4 on a four-point scale); 10 patients had mitral regurgitation after valvotomy (six with grade 1, three with grade 2, one with grade 3; mean, 0.8).

Hemodynamic determination of mitral half-time. Simultaneous LA and LV pressure tracings were obtained with fluid-filled catheters, and a pulmonary artery catheter was used to obtain cardiac output by thermodilution. $\Delta p_0$ was taken as the maximal early diastolic transmitral pressure gradient, and $T_{1/2}$ was measured directly from the LA and LV tracings as the time required for this gradient to fall by half. Hemodynamic data were used rather than Doppler derived half-time data because they are available continuously throughout the valvotomy procedure. The close correlation of Doppler and hemodynamic derivation of $T_{1/2}$ has recently been confirmed. The MVA was calculated both by...
the Gorlin equation (with empiric constant of 38.5)\textsuperscript{19} and by echocardiographic planimetry.\textsuperscript{20} As an overall assessment of the hemodynamic effects of valvotomy, paired \(t\) tests were used to compare the measures before and after valvotomy of heart rate, cardiac output, stroke volume, observed \(T_{1/2}\), initial pressure gradient, MVA (Gorlin), and MVA (planimetry).

Equation 1 was used to predict \(T_{1/2}\) from observed valve areas before and after valvotomy. These predictions were compared with the observed hemodynamic \(T_{1/2}\) by linear correlation. Four correlation coefficients were thus calculated from these data: observed \(T_{1/2}\) versus 220/(Gorlin MVA) and observed \(T_{1/2}\) versus 220/(planimetry MVA), each calculated before and after valvotomy.

**Application of Half-Time Theory to Patients Undergoing Valvotomy**

**Compliance calculation.** To apply our theoretical expression for \(T_{1/2}\) to the patients undergoing valvotomy, it was necessary to estimate the variables used on the right side of Equation 9. Mean LA and LV compliance were calculated as follows: in keeping with the schematic anatomy of our mitral flow model, the “left atrium” was considered to include the pulmonary veins in a common elastic chamber, receiving all of the cardiac stroke volume from the right ventricle during systole and discharging it passively into the LV during diastole. Mean LA+PV compliance was thus obtained by dividing the systolic rise in LA pressure into the cardiac stroke volume. Stroke volume was obtained by dividing thermodilution cardiac output by heart rate. When the right atrial pressure tracing demonstrated significant tricuspid regurgitation, cardiac output was obtained by the Fick or green dye method. Similarly, the mean LV compliance was estimated as the diastolic rise in LV pressure divided into the stroke volume (Figure 2). From these estimates of LA and LV compliance, mean net compliance was calculated as \(C_a/C_s/(C_a + C_s)\).

Initial pressure gradient (\(\Delta p_b\)) was taken as the maximal early diastolic gradient. The coefficient of orifice contraction was taken from the in vitro data, and MVA was defined both by the Gorlin equation and echocardiographic planimetry.

**Comparison of observed half-time to predictions of Equations 1 and 9.** From the measured values of MVA (Gorlin and planimetry), initial pressure gradient, and net chamber compliance (and using coefficient of orifice contraction defined by the in vitro experiments), predicted values of \(T_{1/2}\) were calculated with Equation 9 for individual patients. These predictions for \(T_{1/2}\) were correlated to the observed \(T_{1/2}\) measured directly from the hemodynamic tracings before and after valvotomy, and these correlation coefficients compared with those observed earlier for the empirical prediction for \(T_{1/2}\) (obtained with Equation 1).

**Covariance of pressure and chamber compliance.** It is critical to recognize that the only difference between Equations 1 and 9 is the replacement of the empirical constant 220 in the numerator of Equation 1 by the expression 11.6\(C_a\sqrt{\Delta \bar{P}_e/C_s}\), derived theoretically. If 11.6\(C_a\sqrt{\Delta \bar{P}_e/C_s}\) were to equal 220 under all physiological and pathological conditions, then Equations 1 and 9 would be functionally identical. For this to occur, changes in net chamber compliance and initial pressure gradient would have to be precisely balanced in opposite directions. Therefore, it is essential to examine the behavior of 11.6\(C_a\sqrt{\Delta \bar{P}_e/C_s}\) across a range of patients and before and after valvotomy to assess the theoretical usefulness of Equation 1.

Thus, with the previously observed net compliance and pressure gradient data, the quantity 11.6\(C_a\sqrt{\Delta \bar{P}_e/C_s}\) was calculated for each patient before and after valvotomy, and this was compared graphically with 220. A paired \(t\) test was performed on 11.6\(C_a\sqrt{\Delta \bar{P}_e/C_s}\) to determine its change with valvotomy.

**Atrial and ventricular pressure-volume relations.** Finally, we sought a semiquantitative measure of

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**Figure 2. Method of calculating mean left atrial (LA) and left ventricular (LV) compliance shown before and after valvotomy.** Left atrium was considered to include the pulmonary veins in a common elastic chamber and to receive the full stroke volume during ventricular systole. Thus, mean LA compliance was obtained by dividing systolic rise in LA pressure (\(\Delta P_{LA}\)) into stroke volume and LV compliance obtained by dividing diastolic rise in LV pressure (\(\Delta P_{LV}\)) into stroke volume.
the average atrial and ventricular pressure-volume relations for the group of patients as a whole undergoing valvotomy. The relation between mean compliance and pressure was studied by fitting LA compliance (vs. LA-LV cross-over pressure) and LV compliance (vs. end-diastolic pressure) to a general power-law function $C = A_0 p^{-A_1}$ before and after valvotomy. If the fitting constants ($A_0$ and $A_1$) that were obtained before and after valvotomy were not statistically different from each other, this was taken as evidence that observed compliance changes with valvotomy reflected a translation along a single pressure-volume curve rather than a shift in the curve itself, and the data were then pooled. An approximate pressure-volume curve could then be obtained by integrating the fitted compliance function (here for the LA): $C = \int_0^p V_0 dp = A_0 p^{-A_1} \ln(1-A_1)$ so $V_0 = \int_0^p A_0 p^{-A_1} dp = A_0 p^{1-A_1} / (1-A_1) + K$.

The constant $K$ may be thought of as the volume of the LV or the LA + PV at zero pressure, but this was not explicitly solved for. Because the expressions for LA and LV compliance could be expected to be accurate only throughout the range of pressures observed, the derived $V_0(p_0)$ and $V_0(p_v)$ gave only relative volumes. Nevertheless, they provided information on the average shifts along the atrial and ventricular pressure-volume curves brought about by valvotomy. It was also possible to combine them and calculate net compliance throughout an average diastolic filling period. This was used to assess one of the simplifications used in the analytical formulation of $T_{1/2}$, that net compliance is constant.

### Results

**In Vitro Model**

Relative importance of convective versus viscous resistance in valvular stenosis. Figure 3 displays the LA-LV pressure-decay curve from a representative experiment with the in vitro model for a valve area of 1.50 cm², $C_a$ of 51.0 cm³/mm Hg, $C_v$ of 66.5 cm³/mm Hg (C_n of 28.9 cm³/mm Hg), and $\Delta p_o$ of 5.1 mm Hg. The best-fitted curve of the form predicted by Equation 8, $(A_0 - A_1 t)^{t^2}$, is shown, which demonstrates excellent correlation with the observed decay. Also shown is the best-fitted exponential curve $(A_0 e^{-A_1 t})$, which is the form expected if viscous resistance were predominant. Although the general shape of the exponential curve is similar to the observed decay, the fit is not as good as that obtained with the predicted parabolic form.

For 19 different combinations of MVA, initial pressure gradient, and net chamber compliance, mean correlation of the predicted parabolic form fitted to the observed pressure decay was $r = 0.9982$. A general second-order polynomial curve fit this data with a minimally better correlation ($r = 0.9987$) but a poorer $F$ value (94481 vs. 70704, $p = 0.05$) due to the additional degree of freedom in the general second-order model. The optimal fit of the general exponential form averaged $r = 0.977$, which is significantly ($p < 10^{-4}$) poorer than the parabolic fit. $F$ for this fit was also significantly less than the parabolic fit ($F = 6767, p < 0.001$). Thus, the in vitro data demonstrate conclusively that for stenotic orifices at physiological flow rates, convective resistance predominates, and viscous effects may be neglected without loss of accuracy.

**Determination of the coefficient of orifice contraction.** For these 19 pressure-decay curves, the coefficient of orifice contraction averaged 0.74. There was a gradual increase in the coefficient of orifice contraction with increasing orifice area ($c_v = 0.70 + 0.033 \cdot MVA; r = 0.82, p < 0.01$), which was independent of chamber compliance.

**Ability of the proposed theoretical model to predict pressure half-time.** Figure 4 displays the variability of $T_{1/2}$ with initial pressure gradient for a single orifice size (0.75 cm²) and two levels of net compliance (16.3 and 28.9 cm³/mm Hg). Throughout a range of $\Delta p_o$ from 0.5 to 11.3 mm Hg, the observed $T_{1/2}$ varied more than sixfold. This variation, however, was well explained by the predicted dependence of $T_{1/2}$ on the square root of the initial pressure gradient ($r > 0.99$ for each level of compliance). The traditional formulation ($T_{1/2} = 220/MVA$) predicted a constant $T_{1/2}$ across the full range of pressure and compliance (horizontal line in the figure). The known initial pressure gradient, net chamber compliance, and MVA from 19 in vitro, experiments were used in Equation 9 to predict $T_{1/2}$, which demonstrated excellent agreement with the observed $T_{1/2}$ (Figure 5).

It should be noted that most of the observed in vitro $T_{1/2}$ were above the usual clinical range due to the nonphysiologically high LA and LV compliance used in the model. Thus, the results of the in vitro modeling should be taken as verifying the theoretical predictions of Equations 8 and 9, not as a simple guide relating clinically observed $T_{1/2}$ with MVA. There were, however, combinations of pressure
and compliance for which 220/MVA gave an accurate estimate of T₁/₂ (i.e., the three lowest pressures). This accuracy was achieved when the factor 11.6Cₙ√ΔPₒ/Cₙ was closest to the empirical factor 220. That previous patient studies have shown Equation 1 to be accurate suggests that this fortuitous combination of pressure and compliance commonly occurs in the clinical setting.

**Patients Undergoing Valvotomy**

**Observed variables.** Table 1 lists the mean hemodynamic variables for the 18 patients with mitral stenosis undergoing percutaneous mitral valvotomy. Peak and mean pressure gradient both fell significantly, whereas cardiac output and stroke volume both rose. Average MVA approximately doubled with valvotomy as assessed by the Gorlin equation and echocardiographic planimetry, and these two assessments of valve area were correlated with each other (r = 0.79 before valvotomy, r = 0.67 after valvotomy, p < 0.001). The observed T₁/₂ fell from 241 to 119 msec (p < 0.001).

**Comparison of observed half-time with prediction of 220/MVA.** Included in Figure 6 are data displaying the observed T₁/₂ before valvotomy with predictions based on Equation 1 (squares) with the Gorlin equation (Figure 6A) and planimetered MVA (Figure 6B). The correlations (r = 0.48 for the Gorlin-derived T₁/₂ and r = 0.64 for the planimeter-derived data) were significant (p < 0.05). After valvotomy (Figures 6C and 6D), there was essentially no correlation between the observed T₁/₂ and 220/MVA with Gorlin-derived MVA (Figure 6C; r = 0.28, p = NS) and planimeter-derived MVA (Figure 6D; r = 0.05, p = NS). These correlations are summarized in Figure 7.

**Application of Half-Time Theory to Patients Undergoing Valvotomy**

Atrial, ventricular, and net mean compliance. Table 1 shows that with the fall in peak LA pressure after valvotomy, mean LA (+ PV) compliance rose by 106% (p < 0.02). With increased LV filling, mean LV compliance decreased after valvotomy by 24%, but this was not statistically significant. When mean net compliance was calculated before and after valvotomy [Cₙ = CₑCₒ/(Cₑ + Cₒ)], the rise in Cₑ overshadowed the fall in Cₒ so that Cₙ rose by 42% (p < 0.02).

**Comparison of predicted with observed mitral half-time.** From these compliance and pressure data, T₁/₂ was predicted on the basis of Equation 9 and compared with the observed T₁/₂. Figure 6 shows these predictions in comparison with those with 220/MVA, again with data before valvotomy in Figures 6A and 6B, data after valvotomy in Figures 6C and 6D; Gorlin-derived MVA in Figures 6A and 6C and planimeter-derived MVA used in Figures 6B and 6D. Summary comparisons are in Figure 7.

The theoretical calculation of T₁/₂ before valvotomy (Figures 6A and 6B) was significantly better than that predicted by 220/MVA. After valvotomy (Figures 6C and 6D), the correlation between the observed and theoretical prediction of T₁/₂ was worse than before valvotomy but still better than that from Equation 1. The poorer correlation after valvotomy was due in part to the lower variance of the observed T₁/₂ after valvotomy. In fact, the standard error of the estimate was better after valvotomy, from 38.8 to 26.7 msec for the estimate derived from Equation 9 (compared with 86.1 to 42.5 msec for Equation 1).

**Relation of pressure to compliance and invariance of 11.6Cₙ√ΔPₒ/Cₙ.** An important point to recall is that the difference between Equations 1 and 9 is
neither the effect of pressure gradient nor compliance alone but rather the product $11.6 C_n \sqrt{\Delta p / c_c}$. Table 1 demonstrates that with valvotomy, the doubling in LA compliance dominated the trend toward lower LV compliance so that net compliance rose by 42%. Simultaneously, however, peak pressure gradient was significantly lowered by 36%. Thus, the product $C_n \sqrt{\Delta p}$ increased insignificantly by only 9% so that average changes in compliance and peak pressure gradient largely offset each other. Nevertheless, although pressure and compliance shifts were offsetting on average, there was wide variability in individual patients, leading to the poor predictive accuracy of 220/MVA in Figures 6 and 7.

Figure 8 displays net chamber compliance plotted against initial pressure gradient with points before and after valvotomy connected. Also shown are contours where $11.6 C_n \sqrt{\Delta p / c_c}$ equals 100, 200, 220, and 300. The points lying closest to the 220 contour are those in which Equation 1 would be expected to be most accurate. Most of the points lie between 150 and 250, but there are a few outliers both before and after valvotomy.

Estimation of left atrial and left ventricular pressure-compliance relations. With a power-law model for compliance versus pressure ($C = A_p p^{-A}$), mean LA compliance was found to be strongly dependent on LA-LV cross-over pressure as $C_L = 109 p^{-1}$ ($r=0.87$, $p<0.0001$; Figure 9A), whereas LV compliance was less strongly related to LV end-diastolic pressure: $C_V = 19.4 p^{-1/2}$ ($r=0.61$, $p<0.0001$; Figure 9B). Each relation held equally well before and after valvotomy without significant change in the fitting coefficients, suggesting that the changes in compliance observed with valvotomy simply reflect movement along pressure-volume curves: to the right (steeper portion of the curve) for the LV and to the left (less steep) for the LA, rather than any major change in the material properties of the chambers.

Integrating the above compliance expressions yielded the following approximate pressure-volume relations (neglecting the additive constant):

\[ V_n = \int 109 / p dp = 109 \ln(p) \]  
\[ V_n = e^{109 / p} \]  
\[ V_n = 19.4 \sqrt{p} \]  
\[ V_n = (V_1 / 38.8)^2 \]  

These curves are plotted in Figures 10A and 10B along with indications of how the chambers shift on these curves after valvotomy, the atrium moving to a lower, more compliant zone and the ventricle moving to a higher, somewhat stiffer zone. Again, the absolute volumes along the x axes are not to be taken literally, only the relative shifts.

When Equations 10 and 11 are used to plot instantaneous atrial and ventricular compliance during a typical diastolic filling period (Figures 11A and 11B), it is seen that both of these changes rather significantly, apparently in violation of one of our simplifying assumptions in deriving $T_{12}$, that of using mean compliance rather than instantaneous compliance. Note, however, that LA and LV compliance change in opposite directions during diastolic filling and that net compliance, also displayed in the figures, is almost constant.

### Table 1. Summary Data for Percutaneous Mitral Valvotomy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before valvotomy</th>
<th>After valvotomy</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td>85.2 ± 3.8</td>
<td>81.3 ± 3.3</td>
<td>0.117</td>
</tr>
<tr>
<td>Cardiac output (l/min)</td>
<td>4.1 ± 0.3</td>
<td>4.7 ± 0.3</td>
<td>0.017</td>
</tr>
<tr>
<td>Stroke volume (cm$^3$/beat)</td>
<td>49.3 ± 3.9</td>
<td>58.7 ± 3.1</td>
<td>0.005</td>
</tr>
<tr>
<td>$\Delta p_0$ (mm Hg)</td>
<td>30.8 ± 1.8</td>
<td>19.6 ± 1.6</td>
<td>0.001</td>
</tr>
<tr>
<td>mean $\Delta p$ (mm Hg)</td>
<td>17.9 ± 1.5</td>
<td>5.8 ± 0.6</td>
<td>0.0001</td>
</tr>
<tr>
<td>Gorlin MVA (cm$^2$)</td>
<td>0.84 ± 0.07</td>
<td>1.82 ± 0.12</td>
<td>0.0001</td>
</tr>
<tr>
<td>Echo MVA (cm$^2$)</td>
<td>0.95 ± 0.09</td>
<td>1.75 ± 0.11</td>
<td>0.0001</td>
</tr>
<tr>
<td>Observed $T_{12}$ (msec)</td>
<td>241.6 ± 28.0</td>
<td>119.4 ± 7.2</td>
<td>0.0001</td>
</tr>
<tr>
<td>220/Gorlin MVA (msec)</td>
<td>296.1 ± 30.5</td>
<td>131.7 ± 10.7</td>
<td>0.0001</td>
</tr>
<tr>
<td>220/Echo MVA (msec)</td>
<td>268.8 ± 26.9</td>
<td>141.4 ± 12.0</td>
<td>0.0001</td>
</tr>
<tr>
<td>$C_n$ (cm$^3$/mm Hg)</td>
<td>3.5 ± 0.3</td>
<td>7.2 ± 1.2</td>
<td>0.016</td>
</tr>
<tr>
<td>$C_n$ (cm$^3$/mm Hg)</td>
<td>10.0 ± 2.2</td>
<td>7.6 ± 0.6</td>
<td>0.23</td>
</tr>
<tr>
<td>$C_n$ (cm$^3$/mm Hg)</td>
<td>2.4 ± 0.2</td>
<td>3.4 ± 0.4</td>
<td>0.011</td>
</tr>
<tr>
<td>$11.6C_n \sqrt{\Delta p / c_c}$</td>
<td>190.5 ± 18.6</td>
<td>208.3 ± 16.1</td>
<td>0.34</td>
</tr>
<tr>
<td>Equation 9 (Gorlin)</td>
<td>293.4 ± 30.6</td>
<td>121.9 ± 7.4</td>
<td>0.0001</td>
</tr>
<tr>
<td>Equation 9 (Echo)</td>
<td>234.7 ± 36.9</td>
<td>120.9 ± 6.0</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

All values are mean ± SEM, n = 18 patients.

$\Delta p_0$, peak transmural gradient; mean $\Delta p$, mean transmural gradient; Gorlin MVA, mitral area derived from Gorlin equation; echo MVA, mitral area derived from echocardiographic planimetry; $T_{12}$, mitral pressure half-time; 220/Gorlin MVA, predicted $T_{12}$ with Equation 1 with Gorlin valve areas; 220/Echo MVA, predicted $T_{12}$ with Equation 1 and planimetered valve areas; $C_n$, mean left atrial compliance; $C_n$, mean left ventricular compliance; $C_n$, mean net chamber compliance; $c_c$, coefficient of orifice contraction; $11.6C_n \sqrt{\Delta p / c_c}$, factor by which Equation 9 differs from Equation 1; Equation 9 (Gorlin), predicted $T_{12}$ with Equation 9 and Gorlin valve areas; Equation 9 (Echo), predicted $T_{12}$ with Equation 9 and planimetered valve areas.

All $p$ values are for two-tailed, paired $t$ tests.
Discussion

During the past 4 decades, a number of measurement tools have been described to assess the severity of mitral stenosis, including the Gorlin equation, echocardiographic planimetry, and \( T_{1/2} \). Although it is widely recognized that these methods are imperfect, in general they have been adequate to aid clinical decision making regarding indications and timing of valve replacement surgery. However, when assessing the short- and long-term results of percutaneous mitral valvotomy, improved accuracy is desirable as patient selection criteria concerning this technique become refined.

\( T_{1/2} \) as defined by Doppler echocardiography is an attractive method for the serial evaluation of patients undergoing percutaneous mitral valvotomy. As initially described by Hatle and colleagues,\(^{11}\) it is relatively easy to perform and can be obtained on most patients with mitral stenosis. Before it can be widely applied to patients undergoing valvotomy, however, its validity must be confirmed in this setting.

Accuracy of Traditional Half-Time Formulation in Acute Mitral Valvotomy

In this study, we demonstrated that the traditional formulation of \( T_{1/2} \), which predicts that \( T_{1/2} \) and MVA are inversely proportional to each other and independent of other hemodynamic variables, is inaccurate in the setting of acute valvotomy. Before valvotomy, there was a rough correlation between predicted and observed \( T_{1/2} \), ranging from \( r = 0.48 \) to 0.64 for valve area defined by the Gorlin equation or planimetry, respectively. In the immediate period after valvotomy, there was essentially no correlation between observed \( T_{1/2} \) and 220/MVA regardless of how MVA was measured (\( r = 0.05-0.28 \)).

These data strongly suggest that \( T_{1/2} \) is determined by more than a simple inverse relation with MVA and that change in these other hemodynamic factors with valvotomy contributes to the breakdown of this inverse relation seen after valvotomy.

Theoretical Derivation of Mitral Pressure Half-Time

As we have recently described,\(^4\) the theoretical determinants of \( T_{1/2} \) can be obtained by a straightforward fluid dynamics model of the LA, LV, and mitral valve. This formulation suggests (Equation 9) that \( T_{1/2} \) is indeed inversely proportional to effective valve orifice area but also directly proportional to net LA and LV compliance and proportional to the square root of the initial transmitral pressure gradient.
FIGURE 7. Diagrams of summary of results from half-time (T_{1/2}) predictions. Mitral valve area (MVA) predictions derived from the Gorlin equation are shown in Panel A and those derived from planimetry are in Panel B. In each diagram, the observed T_{1/2} before and after valvotomy (showing mean±SEM) are shown on the left, with theoretical predictions from Equation 9 shown in the middle and predictions from 220/MVA shown on the right. Correlations between respective data sets are also shown. In every instance, the theoretical prediction of T_{1/2} was better than that based on Equation 1.

In vitro testing of theoretical formulation. Several aspects of our mathematical formulation for T_{1/2} were tested in the in vitro model:

1) Is viscosity negligible in stenotic flow compared with convection effects? This was confirmed by the excellent fit to the data of the predicted parabolic decay curve rather than an exponential curve that would result if viscosity were dominant. This assumption is also used in the Gorlin formulation of mitral area evaluation and is implicit in the use of the simplified Bernoulli equation (Δp = 4v^2) in clinical Doppler echocardiography.  

2) What is the coefficient of contraction in stenotic valves? This averaged 0.74 across the range of orifice area from 0.5 to 2.5 cm^2. This value is close to previously published results. Segal and colleagues found an average value of 0.8 for an in vitro model of aortic stenosis. It also corresponds well to the empirical constant of 38.5 widely used in applying the Gorlin equation. Expressed in the units of the Gorlin equation, a coefficient of contraction of 0.74 is equivalent to an empiric constant of 37.3.

3) How do the traditional and theoretical formulations for T_{1/2} compare in predicting T_{1/2}? There is no doubt about the validity of Equation 9 from the in vitro data. T_{1/2} predictably varies inversely with MVA and directly with chamber compliance and the square root of the driving pressure. The equation T_{1/2} = 220/MVA is valid only for the fortuitous combination of pressure and compliance where C_v√Δp_o = 14.8 (i.e., 14.8 · 11.6/c_v = 220). The fact that Equation 1 has worked as well as it has in clinical studies indicates that this combination of compliance and pressure must be roughly correct in the typical mitral stenosis case. Indeed, Nakatani and others recently postulated decreased LV compliance in ischemic heart disease as the cause for a lower than expected T_{1/2} in one patient.

Use of Mitral Valvotomy to Study Mitral Half-Time

Percutaneous mitral valvotomy provides a fortuitous experimental model for studying the determinants of the T_{1/2}. In this procedure, a single primary intervention, the dilation of the mitral valve orifice, induces a cascade of secondary effects: reduction in LA size and pressure, increase in forward stroke volume, reduction in transmural gradient, and reduction in T_{1/2}. From available clinical hemodynamic tracings, we were able to measure initial pressure gradient and MVA (Gorlin and planimetry) and to derive approximations to net chamber compliance. From these data, Equation 9 was used to obtain predictions for T_{1/2}, which were then compared with
FIGURE 9. Plots of left atrial (LA) and left ventricular (LV) compliance curves. Figure 9A shows mean LA (+PV) compliance plotted against LA-LV cross-over pressure before (+) and after (x) valvotomy along with the best-fitting curve of the form $A_p^{+A_t}$, here $109p^{-1}$. Because the variables $A_0$ and $A_t$ were statistically indistinguishable before and after valvotomy, it appears that compliance changes with valvotomy reflect shift along a pressure-volume curve, rather than a change in the intrinsic properties of the atrial wall. Figure 9B shows LV compliance data along with the best power-law fit, $19.4p^{-1/2}$.

$T_{1/2}$ measured directly from the tracings and with the predictions of 220/MVA.

Accuracy of Equation 9 for predicting mitral half-time in vivo. Whether measurements were taken before or after valvotomy and whether MVAs derived from the Gorlin equation or echocardiographic planimetry, our theoretical formulation provided an estimate of $T_{1/2}$ that was superior to 220/MVA. The use of Gorlin as compared with echocardiographically planimetered MVA had no significant influence on the accuracy of either equation. Significantly better correlations, however, were obtained before than after valvotomy for Equations 1 and 9. This is due in part to the lesser variance in the observed $T_{1/2}$ after valvotomy and also likely reflects some breakdown in the simplifying assumptions made to obtain an analytical expression for $T_{1/2}$ (in particular, that M, representing mitral valve and blood inerterance in Equation 2, is ignored and that active LV relaxation is not considered).

Covariance of initial pressure gradient and net chamber compliance and relative invariance of $11.6C_n\sqrt{\Delta p}/c_e$. Note that whereas 220/MVA provided only a fair estimate of $T_{1/2}$ in individual patients before valvotomy and a poor estimate afterward, the average $T_{1/2}$ derived from this expression was only slightly higher than the observed average $T_{1/2}$ both before and after valvotomy. The implication of this is that on-average changes in initial pressure gradient tend to be offset by opposite changes in net chamber compliance so that the scaling constant $11.6C_n\sqrt{\Delta p}/c_e$ is relatively invariant. Thus, when initial pressure gradient and net chamber compliance are plotted on the same graph (Figure 8), the points tend to cluster around the contour $11.6C_n\sqrt{\Delta p}/c_e=190$ before valvotomy, shifting upward slightly to $11.6C_n\sqrt{\Delta p}/c_e=208$ afterward. These values were reasonably close to the
**Net chamber compliance is constant throughout diastole.** This at first seems to be an insupportable assumption because our analysis of compliance before and after valvotomy shows that both LA and LV mean compliance vary with chamber pressure and thus should change during the course of diastole. However, we showed that these compliance shifts during diastole were in opposite directions, and net compliance was in fact almost constant (Figure 11).

Furthermore, it appears to be possible to test whether net compliance is constant throughout diastole by simple observation of the Doppler mitral-inflow pattern. Note that the major consequence of net compliance being constant is that the resulting pressure-decay curve is parabolic in shape, \( \Delta p \approx (A_0 - A_1) t^2 \). But by the Bernoulli equation, transmitral velocity is proportional to the square root of this pressure, \( v \approx (A_0 - A_1) t \), and thus would be linear for a parabolic pressure decay. Thus, when the observed Doppler velocity curve is a straight line, net LA-LV compliance must be essentially constant. When the curve is concave upward, net chamber compliance would be expected to rise during diastole (i.e., that the increase in LA compliance is greater than the decrease in LV compliance), whereas if the curve is concave downward, net chamber compliance should be falling in diastole (LV compliance decrease dominating LA compliance increase).

**Left atrium includes pulmonary veins in common elastic chamber.** That the LA includes pulmonary veins in common elastic chamber is actually not too unreasonable an assumption. Hirakawa and others have recently evaluated the LA and pulmonary veins in the dog and found their compliance to be well described as a single lumped variable. Like our patients undergoing valvotomy, they observed an exponential pressure-volume relation. Careful Doppler evaluation in normal humans has detected a small secondary filling wave (L wave) resulting from diastolic discharge of the pulmonary veins into the LA. However, in that report, it was noted that even mild mitral stenosis eliminated this secondary wave, implying that the LA and PV were acting as a common chamber. It is, in fact, possible to include the pulmonary veins as a separate lumped variable in the mathematical modeling, but this more complex model can only be solved by computer.

**Active left ventricular relaxation is ignored.** In our simplification of Equations 2, 3, and 4, we have assumed that LV pressure falls to its minimum pressure with mitral valve opening and is in its fully relaxed state. Because the time constant of LV relaxation (T) is much shorter (about 30 msec) than atrial depressurization, this assumption does not greatly affect calculations of \( T_{1/2} \) before valvotomy but may account for some of the error observed in applying Equation 9 after valvotomy. It is straightforward to include active relaxation in the LV

**Simplifying Assumptions and Possible Sources of Error in Valvotomy Patients**

To keep these results in perspective, it is important to examine the implicit and explicit assumptions used in formulating our mathematical approach and possible experimental error.
compliance formulation in Equation 4 as a refinement to our mathematical model; we have used this extension to study the determinants of peak LV filling in dogs.  

Mitral regurgitation is ignored. Because any transmital flow resulting from mitral regurgitation is not included in the forward stroke volume, calculated LA and LV compliances may be artifically low. However, for these 18 patients, mean angiographic mitral regurgitation was only 0.4 before valvotomy and rising to 0.8 after valvotomy (on a semiquantitative 0–4 scale) with only one patient as high as 3+. Furthermore, the pressure-compliance relations for all patients with 2 or 3+ mitral regurgitation (n = 1 before valvotomy, n = 4 after valvotomy) were analyzed as a separate subgroup; these were statistically indistinguishable from the patients with 0 or 1+ mitral regurgitation. The regurgitant volume involved, thus, appears not to have significantly affected calculated compliances.

Assessment of mitral valve area. It is widely recognized that neither echocardiographic planimetry nor the Gorlin line is a perfect measure of MVA. However, each is widely used clinically, and there are no competing methods proven to be superior. We have used both methods in analyzing the observed T1/2 data as a form of internal control; the results obtained were independent of the technique of area measurement.

In vivo pressure measurements. Fluid-filled catheters were used for all pressure measurements because micromanometer recordings were not technically feasible during balloon valvotomy. This may explain some of the poor correlations between predicted and observed T1/2, especially after valvotomy. However, both the empirical Equation 1 and the theoretical Equation 9 used the same observed T1/2 data as a standard of reference. It is unlikely that error in measuring T1/2 would systematically favor Equation 9 over Equation 1, and therefore, the improved correlation seen with the theoretical approach appears to be real.

Summary

We have shown that T1/2 is inaccurate in the setting of acute valvotomy, implying that it depends on hemodynamic variables other than the MVA. We have developed a mathematical description of the dynamics of mital valve flow that predicts that the T1/2 should vary inversely with MVA (the common assumption for its use in clinical cardiology) but also directly with mean net chamber compliance and the square root of the initial pressure gradient. We have shown this mathematical formulation to be highly accurate in an in vitro model in which orifice area, chamber compliance, and initial pressure gradient could be independently adjusted. We have also shown it to be accurate in 18 patients undergoing mitral valvotomy in whom T1/2, initial pressure gradient, MVA, and LA and LV compliance could be measured. We also found that any accuracy of the empiric expression T1/2 = 220/MVA depended on the fortuitous tendency for net chamber compliance and initial pressure gradient to change in opposite directions, thus leading to offsetting effects on T1/2. The recognition of the effect of chamber compliance and transmural gradient on T1/2 warns against relying on it in patients immediately after valvotomy but should be a challenge to develop more sophisticated evaluations of mitral flow.

Acknowledgment

We thank Michael H. Picard, MD, for review of the manuscript.

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KEY WORDS • mitral stenosis • Doppler echocardiography • mathematical models • hemodynamics
Inaccuracy of mitral pressure half-time immediately after percutaneous mitral valvotomy. Dependence on transmitral gradient and left atrial and ventricular compliance.

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_Circulation_. 1988;78:980-993
doi: 10.1161/01.CIR.78.4.980

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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