Noninvasive Assessment of Mitral Inertance: Clinical Results with Numerical Model Validation

MS Firstenberg, NL Greenberg, NG Smedira, PM McCarthy, MJ Garcia, JD Thomas

The Cleveland Clinic Foundation, Cleveland, USA

Abstract

Inertial forces (Mdv/dt) are a significant component of transmirtal flow, but cannot be measured with Doppler echo. We validated a method of estimating Mdv/dt.

Ten patients had a dual sensor transmirtal (TM) catheter placed during cardiac surgery. Doppler and 2D echo was performed while acquiring LA and LV pressures. Mdv/dt was determined from the Bernoulli equation using Doppler velocities and TM gradients. Results were compared with numerical modeling.

TM gradients (range: 1.04-14.24 mmHg) consisted of 74.0±11.0% inertial forces (range: 0.6-12.9 mmHg). Multivariate analysis predicted Mdv/dt=4.171(S/DATIO) +0.063(LAVOLUME_MAX) 2. Using this equation, a strong relationship was obtained for the clinical dataset (y=0.86±0.045, r=0.90) and the results of numerical modeling (y=0.96±0.16, r=0.84).

TM gradients are mainly inertial and, as validated by modeling, can be estimated with echocardiography.

1. Introduction

The estimation of transmirtal flow and pressures gradients are two of the most important applications of Doppler echocardiography for the clinical assessment of LV diastolic function and the evaluation of valvular pathology (1,2). The relationship between transmirtal pressure gradients and flow as measured using Doppler echo is governed by the Bernoulli equation. The complete form of the Bernoulli equation consists of three components, 1) the convective term which describes the kinetic energy of blood as it passes through the mitral valve, 2) the inertial term which describes the pressure gradient that must be applied to accelerate the mass of blood as it moves from the left atrium to the left ventricle, and 3) the viscous term which describes the energy loss secondary to the resistive drag along the walls of the heart. Previous research has demonstrated that the viscous component of intracardiac blood flow can be considered negligible, and when evaluating a stenotic or regurgitant orifice, the inertial term can also be considered negligible relative to the large convective forces (3).

However, for a nonrestrictive orifice such as a normal mitral valve, these assumptions do not apply. Because of the relatively large amount of blood that must pass through a non-restrictive mitral valve with each cardiac cycle the inertial term is presumed to play a significant role in describing the overall transmirtal pressure gradient (4). Although previous investigators have demonstrated the importance of the inertial component of the Bernoulli equation when applied to transmirtal flow, little work has been done to describe it (5, 6). The purpose of the study is to evaluate the inertial component of transmirtal pressure gradients and determine a simple echocardiographic means to estimate its magnitude.

2. Methods

2.1. Patient population

After prior approval by our Institutional Review Board, written informed consent was obtained from 10 patients (8 males, mean age: 65.9±5.9 years) prior to undergoing first time cardiac surgery requiring cardiopulmonary bypass. Pre-operative left ventricular ejection fraction (EF) was normal (EF>50%) in 7, moderately depressed in 4 (EF=35-40%) and severely (EF<25%) depressed in one. All were in sinus rhythm. Surgical procedures performed included isolated coronary artery bypass grafting (CABG) in 6, CABG with septal myomectomy in one, CABG with left ventricular infarct exclusion surgery in one, mitral valve replacement in one, and an aortic valve replacement in one.

2.2. Intra-operative protocol

Following routine induction of general anesthesia, median sternotomy, and pericardiotomy, a dual sensor high fidelity pressure transducer (Millar Instruments, Houston, TX) was positioned from a small right pulmonary vein incision across the mitral valve with one sensor in the LA and the second, 5 cm distal, in the LV. Prior to insertion, all catheters were immersed in warm saline for at least 30 minutes to minimize drift and each individually calibrated to atmospheric zero. Appropriate
times (time to from minimal to peak velocity, $S_{ACC}$, $D_{ACC}$, $AR_{ACC}$), deceleration times (time from peak to minimal velocity, $Sp_{T}$, $D_{PT}$, $AR_{PT}$) and waveform duration ($Sp_{BR}$, $D_{BR}$, $AR_{BR}$). From the LV filling velocities recorded at the tips, peak early (E) and atrial contraction (A) velocities and their corresponding acceleration times ($E_{ACC}$, $A_{ACC}$), deceleration times ($E_{PT}$, $A_{PT}$), and waveform duration times ($E_{BR}$, $A_{BR}$) were also automatically determined using customized software.

2.4. Numerical modeling

A previously described and clinically verified numerical model of the cardiovascular system (8) was used to validate the clinically derived relationship between $\frac{dM}{dt}$ and different physiologic variables. In short, our model is a closed-loop, lumped parameter system based upon 24 first-order differential equations that simulate pressure, volume, and flow throughout the heart and pulmonary and systemic vasculature. Output consists of waveforms corresponding to pulmonary venous flow, transmural flow, left atrial and ventricular volumes in 5 msec intervals for a single complete cardiac cycle. Initial model parameters of LA and LV systolic and diastolic function, similar to those obtained and verified by previous in-vivo and clinical studies were used (9). Total systemic volume was altered (4500 - 6500 ml in 250 ml increments) under varying effective mitral valve area (1.00 - 4.00 cm2) and constant LA and LV systolic and diastolic function to yield a modeled stroke volume that range from 11.5 to 120 ml. For each physiologic parameter modeled, waveforms and volumes were analyzed similar to the analysis performed on the clinical waveforms and volumes. Overall, 35 different conditions were modeled.

2.5. Determination of inertial forces

The measurement of the transmural inertial component was determined by solving for the Bernoulli equation (Equation 1) using the combined results of the simultaneously acquired pulsed Doppler echocardiographic and physiologic data.

Equation 1: $\Delta p(t) \approx \frac{1}{2} \rho A \left( v_2^2 - v_1^2 \right) + M \frac{dv}{dt} + R(v)$

Where $v$ is the blood velocity at the two points of interest ($v_1$ and $v_2$), $\rho$ is blood density (1.05 g/cm$^3$), $M$ is a distributed inertial term reflecting the effective mass of blood being accelerated between the two points. $R(v)$ is a resistive term reflecting the viscous energy loss along the path and is generally considered negligible and hence ignored (3). Transmural pulse Doppler velocities were used to solve for the convective term in which the initial velocity within the left atrium ($v_1$) was considered
negligible ($\Delta P_{\text{CONV}} = \frac{1}{2} \rho v^2$) (3). The instantaneous transmural pressure gradient ($\Delta P_{\text{TM}}$) was determined by subtracting the left atrial pressure from the left ventricular pressure from the digitally recorded pressure data. The inertial component was then determined by subtracting the total convective forces from the total actual transmural pressure gradient (Equation 2).

Equation 2: $\frac{M_d}{dt} = (\Delta P_{\text{TM}} - \Delta P_{\text{CONV}})$

To facilitate a broader clinical application, all pressure and velocities were derived from the corresponding peaks of the pressure and velocity waveforms.

2.6. Statistical analysis

All data are expressed as a mean ± standard deviation. All statistical analyses were performed using Systat 7.0 (SPSS Inc, Chicago, Illinois). Comparison of Doppler parameters and the calculated inertial terms were performed using linear regression analysis. Similar regression analysis was performed on the results of numerical modeling to correlate clinically significant echocardiographic parameters to $\frac{M_d}{dt}$. Stepwise and multivariate regression analysis was used to identify the best determinants of $\frac{M_d}{dt}$ among statistically significant clinical ultrasound parameters. The resulting multivariate coefficients where then used to estimate $\frac{M_d}{dt}$ from both the clinical and numerical modeling results and was assessed with a linear regression analysis. A P-value < 0.05 was considered statistically significant.

3. Results

3.1. Early diastolic inertial forces

Fourteen complete data sets were obtained from 10 patients. Peak $\Delta P_{\text{TM}}$ ranged from 1.04 to 14.2 mmHg (4.81 ± 3.94 mmHg) and corresponding pulsed Doppler early diastolic velocities ranged from 17.7 to 81.3 cm/sec (average: 49.1 ± 15.6 cm/s). By solving for the Bernoulli equation, $\frac{M_d}{dt}$ ranged from 0.6 to 12.9 mmHg (3.40 ± 3.78 mmHg) representing 74.0 ± 11.0 % (range: 55 - 91%) of the peak $\Delta P_{\text{TM}}$. Overall, $\frac{M_d}{dt}$ correlated strongly with $\Delta P_{\text{TM}}$ ($y = 0.76x + 0.073$, r = 0.94). Because no single echocardiographic variable was a strong correlate of $\frac{M_d}{dt}$, the two strongest predictors (Figure 1a-b) were included into a stepwise multiple linear regression analysis which yielded Equation 3:

$\frac{M_d}{dt} = -4.171(S/D \text{ ratio}) + 0.063(\text{LVOL}_{\text{MAX}}) + 5.$
3.2. Numerical modelling

For the 35 different conditions modeled, peak $\Delta P_{m}$ ranged from 3.6 to 12.5 mmHg and calculated $Mdv/dt$ ranged from 3.6 to 7.3 mmHg. Overall $Mdv/dt$ represented 55.2 ± 13.3 % (range: 31.2 – 85.0 %) of the $\Delta P_{m}$. Model maximum LA volume ranged from 45.0 to 202.6 ml and S/D ranged from 0.36 to 1.12. Regression analysis indicated that the relationship between the S/D ratio and LA volume-max and $Mdv/dt$ for the model data was similar to that obtained from the in vivo data. Incorporating these results into the equation derived from the multivariate analysis of the clinical data resulted in a linear relationship (Figure 3). Model predicted $Mdv/dt$ was statistically similar to actual $Mdv/dt$ (p=0.12).

![Graph showing regression analysis results]

4. Conclusions

We have demonstrated through in vivo studies, validated with numerical modeling, that the inertial force contribution to the total early diastolic transmural pressure gradient is significantly greater than the convective force gradient. Through univariate and multivariate regression analysis we also derived a relationship between easy to measure echo variables, specifically the pulmonary venous S/D ratio and the maximum LA volume, and transmural inertial forces thereby allowing for it's routine clinical estimation. Further validation of our in vivo findings with a clinically validated numerical model over a wide range physiologic conditions further supports the concept of applying echo variables for the clinical estimation early diastolic transmural inertial forces and pressure gradients.

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References


Address for correspondence.
Michael S. Firstenberg, M.D.
Department of Cardiovascular Medicine, Desk F15
The Cleveland Clinic Foundation
9500 Euclid Avenue
Cleveland, Ohio 44195 USA
firstem@ccf.org

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