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 transmitral flow, but cannot be measured with Doppler echo. We validated a method of estimating Mdv/dt.

Ten patients had a dual sensor transmitral (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 forcers (range: 0.6-12.9 mmHg). Multivariate analysis predicted Mdv/dt=-4.171(S/D_{RATIO}) +0.063($LA_{VOLUME\text{-}MAX}$)+5. Using this equation, a strong relationship was obtained for the clinical dataset (y=0.98x-0.045, r=0.90) and the results of numerical modeling (y=0.96x-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 transmitral 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 transmitral 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 transmitral pressure gradient (4). Although previous investigators have demonstrated the importance of the inertial component of the Bernoulli equation when applied to transmitral flow, little work has been done to describe it (5, 6). The purpose of the study is to evaluate the inertial component of transmitral 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 anatomical placement was confirmed through the use of transesophageal echocardiography and visualization of appropriate chamber specific waveforms.

Signals were amplified with a universal amplifier (Gould, Valley View, OH) and recorded digitally through a NB-MIO-16 multifunction input/output board (National Instruments, Austin TX) with 12-bit resolution and a sampling frequency of 1000 Hertz. The digital signals were recorded with a customized data acquisition and analysis application developed using LabVIEW (National Instruments, Austin TX) on a standard Pentium-based personal computer running Windows 95.

Transesophageal echocardiography was performed using a Hewlett-Packard Omniplane probe connected to a Sonos 1500 or 2500 echocardiograph (Hewlett-Packard, Andover, MA). For recording of PV spectral Doppler signals, the sample volume was placed in the left upper pulmonary vein at 1 cm from the junction with the LA. The view was optimized to align the PV flow with the cursor. Pulsed Doppler audio signals were acquired and digitized at 20 kHz simultaneously with the pressure measurements by connecting the audio output of the echocardiograph to the above data acquisition apparatus. Pulsed Doppler audio signals were processed using a short-time Fourier analysis (20 kHz sampling frequency with 256 sample width, 128 sample shift per analysis, using a Hamming window) to reconstruct spectral Doppler images and extract the PV velocity profiles (7). Under similar hemodynamic conditions, and using similar digital data acquisition techniques, pulsed Doppler signals were obtained by placing the sample volume in the region of the mitral valve tips.

For each patient, 8 second recordings of intra-cardiac pressure and either PV or transmitral pulsed Doppler velocities were obtained during suspended respiration. Four patients, at the discretion of the operating surgeon, had repeat complete data sets collected during continuous infusion of phenylephrine titrated to a mean aortic pressure of 100 mmHg.

2.3. Data measurements and analysis

For each 8-second physiologic condition measured, 3 representative complete cycle waveforms were analyzed using a customized LabVIEW data analysis application. All Doppler and hemodynamic measurements were performed from the digitally stored signals with analysis performed on the simultaneously aligned cardiac cycles. Then, for each parameter measured, the results of each of the 3 cycle's measurements were then averaged together.

Specifically, from each data set, LA and LV volumes and ejection fraction were determined at end-systole and end-diastole using Simpson's biplane disc method. From the PV flow, systolic (S), diastolic (D) and atrial reversal (AR) velocities were obtained, as well as their respective time velocity integrals (S_{TVI}, D_{TVI}, AR_{TVI}), acceleration times (time to from minimal to peak velocity, S_{ACC}, D_{ACC}, AR_{ACC}), deceleration times (time from peak to minimal velocity, S_{DT}, D_{DT}, AR_{DT}) and waveform duration (S_{DUR}, D_{DUR}, AR_{DUR}). 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_{DT}, A_{DT}), and waveform duration times (E_{DUR}, A_{DUR}) 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 M*dv/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, transmitral 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 intra-operative and clinical studies were used (9). Total systemic volume was altered (4500 – 6000 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 transmitral inertial component was determined by solving for the Bernoulli equation (Equation 1) using the combined results of the simultaneous acquired pulsed Doppler echocardiographic and physiologic data.

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

Where v is the blood velocity at the two points of interest ($v1$ and $v2$), ρ 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 loses along the path and is generally considered negligible and hence ignored (3). Transmitral pulse Doppler velocities were used to solve for the convective term in which the initial velocity within the left atrium ($v1$) was considered negligible ($\Delta P_{CONV} = ½\rho v^2$) (3). The instantaneous transmitral pressure gradient (ΔP_{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 transmitral pressure gradient (Equation 2).

Equation 2: $Mdv/dt \approx (\Delta P_{TM} - \Delta P_{CONV})$

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

2.6. Statistical analysis

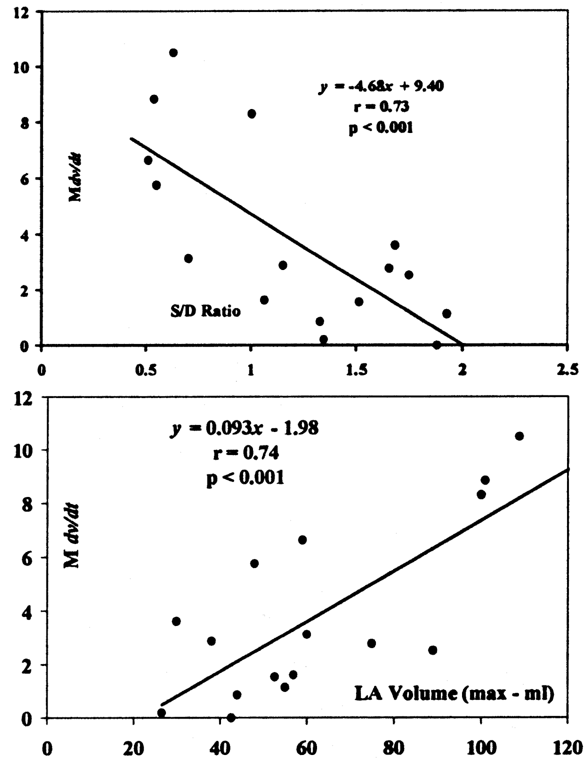
All data are expressed as a mean ± standard deviation. All statistical analyses were performed using Systat 7.0 (SPSS Inc, Chicago, Illinois). Comparison of Doppler parameters and the calculated inertial terms were performed using linear regression analysis. Similar regression analysis was performed on the results of numerical modeling to correlate clinically significant echocardiographic parameters to Mdv/dt. Stepwise and multivariate regression analysis was used to identify the best determinants of Mdv/dt among statistically significant clinical ultrasound parameters. The resulting multivariate coefficients where then used to estimate Mdv/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.

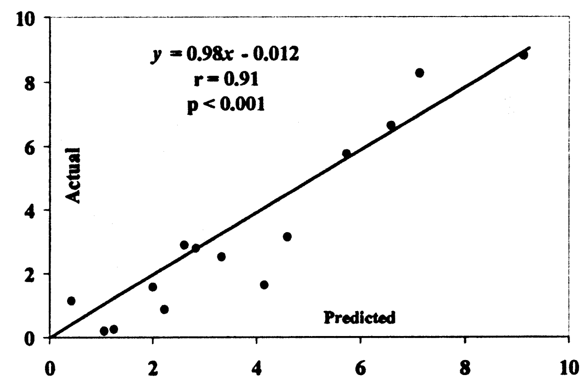
3. Results

3.1. Early diastolic inertial forces

Fourteen complete data sets were obtained from 10 patients. Peak ΔP_{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, M*dv/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 ΔP_{TM}. Overall, M*dv/dt* correlated strongly with ΔP_{TM} (y=0.76x+0.073, r=0.94). Because no single echocardiographic variable was a strong correlate of M*dv/dt*, the two strongest predictors (Figure 1a-b) were included into a stepwise multiple linear regression analysis which yielded Equation 3:

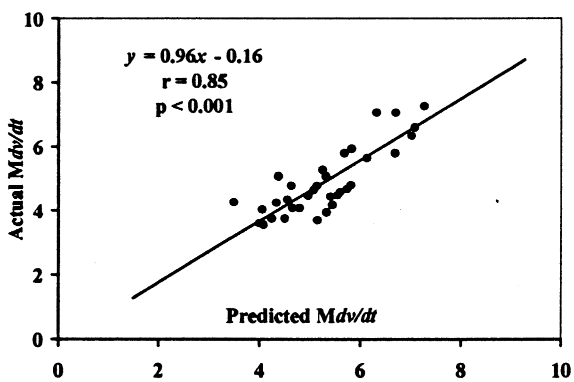
$$Mdv/dt = -4.171(S/D\ ratio) + 0.063(LA_{VOL\text{-}MAX}) + 5.$$





3.2. Numerical modelling

For the 35 different conditions modeled, peak ΔP_{TM} ranged from 3.6 to 12.5 mmHg and calculated M*dv/dt* ranged from 3.6 to 7.3 mmHg. Overall M*dv/dt* represented 55.2 ± 13.3 % (range: 31.2 – 85.0 %) of the ΔP_{TM}. 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 M*dv/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 M*dv/dt* was statistically similar to actual M*dv/dt* (p=0.12).



4. Conclusions

We have demonstrated through *in vivo* studies, validated with numerical modeling, that the inertial force contribution to the total early diastolic transmitral 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 transmitral 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 transmitral inertial forces and pressure gradients.

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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