Intraventricular Pressure Differences
A New Window Into Cardiac Function

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Like all fluids, blood tends to flow from areas of high pressure to low pressure. This seemingly trite observation hides a great deal of sophisticated pathophysiology that we are only beginning to exploit diagnostically and potentially therapeutically. In this issue of Circulation, Yotti and colleagues have exploited a new noninvasive technique to measure the small pressure differences generated within the normal left ventricular outflow tract in systole, demonstrating the utility of such measurements in quantifying ventricular systolic function. Because the fluid dynamics concepts behind these methods remain obscure to many cardiologists, it is worth reviewing the theoretical underpinnings in the hope that they will be more widely applied on the basis of articles like those of Yotti et al and others.

See p 1771

Cardiologists have become comfortable with the use of the Gorlin equation in the cardiac catheterization laboratory and the simplified Bernoulli equation in the echocardiography laboratory to characterize the severity of valvular stenosis. Both equations are based on the principle of conservation of energy, relating the pressure drop (potential energy) across the valve to the rise in velocity (kinetic energy) as blood rushes through it. Several special circumstances combine to make these simple equations particularly applicable to flow through a restrictive orifice, including lack of a significant friction factor (viscosity) and a lack of pressure recovery as the blood rushes out of the abrupt obstruction. One of the most important simplifications is the absence of a significant “inertial” component to flow through a restrictive orifice. That is, the amount of blood actually moving at high velocity is tiny compared with the volume of the overall column of blood in the left ventricular outflow tract. Thus, very little pressure is expended in getting that small mass moving, and all of the potential energy lost across the valve (Δp) is given by the kinetic energy of the blood (4v² in the echo laboratory, if p is in millimeters of mercury and v is in meters per second). This is termed the “convective” component of the Bernoulli equation, which relates to the change in velocity (and pressure) that occurs as blood simply moves—or convects—from a wide region to a narrow region and the change in geometry forces the acceleration.

The simplicity of valvular stenosis changes considerably when one considers the more general situation of flow in the left ventricle. Here, flow is much more complex (inherently 3-dimensional and time variable) and the pressure differences are much smaller, typically <5 mm Hg from base to apex. Nevertheless, it has been known for some time that these intraventricular pressure gradients (IVPG) are crucial for the proper functioning of the cardiovascular system. Ling et al and Falsetti et al were among the first to describe the small pressure differences that drive blood from the mitral valve level into the ventricle during diastole. These small (in general, <5 mm Hg) pressure differences, commonly termed diastolic suction and responsible for efficient filling of the ventricle at low mean left atrial pressure, were shown to be augmented with inotropic stimulation and exercise and decreased with β-blockade and ischemia. Pasipoularides extended these concepts to systolic ejection by measuring pressure differences within the normal left ventricular outflow tract, observing an average peak difference of 6.7 mm Hg at rest, rising to 13.0 mm Hg during submaximal exercise. (Note: As cardiologists we commonly use the term “pressure gradient” where a physicist would use “pressure difference,” reserving the word gradient to describe the rate of change of pressure along a line. For this editorial, I will try to adhere to the physics definition, but readers should be aware that this is not always the case in the cardiology literature.) Importantly, this ejection gradient occurred at the time of peak flow acceleration, not peak flow, indicating that in this nonobstructive geometry, the inertial term of the Bernoulli equation dominates the convective (kinetic energy) term, in contrast to valvular stenosis. Thus, the simplified Bernoulli equation cannot be used to quantify either left ventricular inflow or outflow tract gradients.

This inapplicability of simple Doppler techniques explains in large part why IVPG have been only rarely used in research and never in clinical cardiology. To measure them requires simultaneous high-fidelity pressure measurements with multiple micromanometer catheters placed invasively within the heart, a highly demanding task technically and entirely inappropriate for clinical use. Fortunately, Yotti et al have applied fluid dynamics principles to measure noninvasively ejection intraventricular pressure differences (EIVPD) from color M-mode Doppler data extending concepts originally developed for diastolic IVPG by Thomas, Greenberg, and others from the Cleveland Clinic. To understand how we can measure pressure gradients from velocity data, we start with the “almost” complete Bernoulli equation with both inertial and convective terms.
where $\Delta p$ is the pressure difference between two points, $\Delta(v^2)$ is the change in the square of velocity from one point to another, $\rho$ is blood density (with appropriate units, $\frac{1}{2}\rho$ equates to the constant $4$ in the simplified Bernoulli equation), $\frac{dv}{dt}$ is the instantaneous temporal acceleration of flow through the region, and $M$ is the “effective” mass being accelerated, a negligible quantity for true stenosis, but the dominant term when flow is not obstructed. Indeed, it can be shown that for a minimal diameter $D$, the inertial constant $M$ varies in proportion to $D$, whereas the kinetic term $\frac{1}{2}\rho v^2$ varies inversely to $D^2$. For nonobstructive flow, where pressure changes gradually over a distance, not at a discrete point, we must use the Euler equation, a differential version of the Bernoulli equation for pressure change along a streamline of flow:

$$\frac{\partial p}{\partial s} = -\rho \left( \frac{\partial v}{\partial t} + v \cdot \frac{\partial v}{\partial s} \right),$$

where the inertial and convective terms are in the same order as the Bernoulli equation, but the discrete terms [$\Delta p$ and $\Delta(v^2]$ have been replaced by their spatial derivatives, yielding the rate of pressure change per centimeter of distance along the streamline. To return the total pressure drop between points A and B along the streamline, this equation must be integrated numerically:

$$\Delta p = -\rho \int_{A}^{B} \left( \frac{\partial v}{\partial t} + v \cdot \frac{\partial v}{\partial s} \right) \, ds.$$

Although this looks complicated, note that all we need to solve it is a representation of velocity as a function of space and time [$v(s,t)$] along a streamline of flow, and $v(s,t)$ is precisely what the color Doppler velocity map represents. Of course, the velocity map needs to be smoothed before applying the noise-magnifying partial derivatives, but the computational demands are trivial for a personal computer. The Figure shows schematically how these partial derivatives are summed together to produce the pressure gradient map. One could well question whether the requirement that this velocity be along a streamline is truly met. Fortunately for both diastolic ventricular inflow$^9$ and systolic ventricular outflow$^1$, misalignments as great as 20° produce errors <0.5 mm Hg.

In a previous article, Yotti et al compared their noninvasive estimation of EIVPD with invasive measurements, reporting a correlation of 0.98 and agreement within a standard deviation of <0.3 mm Hg. In their article in this issue, they extend this work by comparing EIVPD with standard invasive pressure gradients. The shows the E-wave from transmitral diastolic inflow (shown after smoothing in the panel above “$v$”), with time along the horizontal axis and distance along the vertical axis, and $\rho$ reflecting positive velocities toward the apex of the heart. $\frac{dv}{ds}$ is the temporal velocity derivative at each point within the panel (red showing positive values and blue negative), whereas $\frac{dv}{ds}$ is the spatial derivative, positive near the mitral valve and negative as the flow decelerates at the apex. Multiplying and summing the derivatives as shown produce the pressure gradient above “$\delta p$/ds,” demonstrating a strong negative gradient early in diastole (“diastolic suction”).

Application of the Euler equation to color M-mode velocity data to measure intraventricular pressure differences. This shows the E-wave from transmitral diastolic inflow (shown after smoothing in the panel above “$v$”), with time along the horizontal axis and distance along the vertical axis, and $\rho$ reflecting positive velocities toward the apex of the heart. $\frac{dv}{ds}$ is the temporal velocity derivative at each point within the panel (red showing positive values and blue negative), whereas $\frac{dv}{ds}$ is the spatial derivative, positive near the mitral valve and negative as the flow decelerates at the apex. Multiplying and summing the derivatives as shown produce the pressure gradient above “$\delta p$/ds,” demonstrating a strong negative gradient early in diastole (“diastolic suction”).

**Figure 1A and 1B in the Yotti et al article.** Although the quality of the original color M-mode data. Whenever spatial or temporal derivatives are applied to discretely sampled data, noise is bound to increase in the process, a fact apparent in Figure 1A and 1B in the Yotti et al article. Although the subsequent spatial integration will smooth out the noise to some degree, it is essential that a complete color M-mode map be obtained before processing. Thus, only future research will tell whether EIVPD becomes an accepted method to measure load-independent contractility or if over time the research community discovers weaknesses not apparent in the Yotti article.

Nevertheless, it is clear that IVPD is a promising general technique that should be pursued vigorously to exploit its full
potential. Already it has proven valuable in assessing diastolic function and understanding the pathophysiological link between systole and diastole. Rovner et al\textsuperscript{12} have validated the noninvasive measurement of diastolic IVPD in the complex anatomy of hypertrophic cardiomyopathy and then showed significant increases in diastolic suction (from 1.5 to 2.6 mm Hg) after alcohol septal reduction therapy. The same group has also recently shown in heart failure patients that the ability to augment diastolic suction with exercise is the best predictor of maximal oxygen consumption, with a correlation of 0.8 between the exercise-induced increase in diastolic IVPD and $\text{VO}_2\text{max}$.\textsuperscript{14} Preliminary work has shown that normal aging blunts the observed augmentation in diastolic IVPD seen with preload increases,\textsuperscript{15} but that lifelong endurance exercise training partially ameliorates this effect.\textsuperscript{15} One of the many potential applications of EIPVD in the notoriously difficult arena of noninvasive quantification of systolic function applied to such problems as assessing contractile reserve in questions of myocardial viability or testing the contractile reserve of the left ventricle. To exploit these important developments in both systolic and diastolic IVPD, it is essential that manufacturers of echocardiography instruments develop on-line and off-line tools that will allow these calculations to be made rapidly and automatically on clinical data.

In summary, the approach used by Yotti et al to derive regional pressure differences within the ventricle appears to be a powerful new tool for both clinical assessment of ventricular systolic and diastolic function and research investigation of the pathophysiology of ventricular function. It is simply the latest in a long line of technical advances that have expanded the diagnostic value of echocardiography and kept it the premiere modality in cardiovascular imaging.

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**References**


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