

Advanced Fluid Dynamics in Echocardiography

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INTRODUCTION

Echocardiography is an integral part of cardiac assessment providing quantitative and qualitative evaluation techniques reflecting cardiac function. It has enjoyed a leading role since inception and is the favored method to evaluate ventricular function and valvular pathology. Its ability to characterize cardiac performance without use of ionizing radiation, bedside application, and relatively low cost has contributed to the expanding role of echocardiography in clinical medicine [1]. This expansion includes new modalities, such as the addition of contrast agents and situational applications based on mathematical modeling.

A thorough understanding of fluid dynamic principles is critical to the quantitative application of echocardiography and its application to cardiovascular structure and function. This defines the relationships between hematologic properties, velocities, flow, and pressure gradients. In addition to an understanding of governing principles, one must also appreciate both the basic and situational assumptions – including their inherent limitations - as echocardiography is used in an ever-expanding range of applications.

DOPPLER EFFECT

Integral to echocardiography is the ability to translate sound waves into clinically relevant information by applying basic principles of ultrasonography. One of these principles is the Doppler effect. This refers to the change in an observed sound wave frequency due to motion. This motion can be attributed to the source, observer or reflection from an object in motion. The Doppler effect serves a key role in a many applications ranging from weather forecasting, astronomy, and assessing automotive speed. In the case of ultrasound Doppler, the source and observer are contained within the transducer probe and frequency shifts are due to reflections off tissues. The Doppler shift (Equation 1) is calculated from the frequencies collected via the transducer [2], this is calculated as:

Equation 1:
$$f_d = f_t - f_r = f_t * 2 * \frac{u * \cos \theta}{c}$$

Where f_d is the Doppler shift, f_t is the transmitted frequency, f_r is the returning frequency, c is the speed of the ultrasound wave and $u * \cos \theta$ is the velocity component of the reflection in the direction of the ultrasonic beam. The angle θ is measured between the line of movement of the reflector and the transducer beam. The Doppler image begins to degrade above an angle of 70° as $\cos \theta$ approaches 0 which occurs at 90°. Since the exact angle is often unknown, Doppler outputs are interpreted as the Doppler shift rather than a velocity. This shift is then processed and can be interpreted via frequency analyzer, a speaker as an audible output or a spectrogram as a visual portrayal of the Doppler shift.

Several methods of interpreting Doppler data exist which allow for velocity estimations. The most commonly utilized is the spectrum analyzer [3]. In this method, an angle correction is applied to the Doppler shift that produces a range of velocities. These spectrograms are generally utilized to estimate time between events, waveform analysis, or maximal velocities (i.e. during cardiac systole or diastole). All Doppler ultrasounds are equipped with predetermined electronic gating which determines the depth at which they interpret data and Doppler shift allowing for increased or decreased penetration and clarity. Current applications of Doppler principles include continuous wave, pulsed wave, high repetition frequency, and color flow. A variety of image manipulation technologies – such as Power Doppler and Harmonics – are being investigated for potential improvement in imaging characteristics. Doppler beams are affected by attenuation, refraction, speed of sound variation, and defocusing. These factors can interfere with clinical examinations to varying degrees depending on which modality is utilized.

In continuous wave ultrasound, waves are generated with a continuous cyclic electrical signal. As the waves disperse through tissue and encounter moving structures, they undergo a shift in wave frequency that returns to the detector (Figure 1). This is distinguished from the underlying surface static due to the difference in frequency. Movements towards the transducer result in an increased frequency while objects moving away from the transducer result in a decreased frequency. These subtle changes in frequency result in image generation.

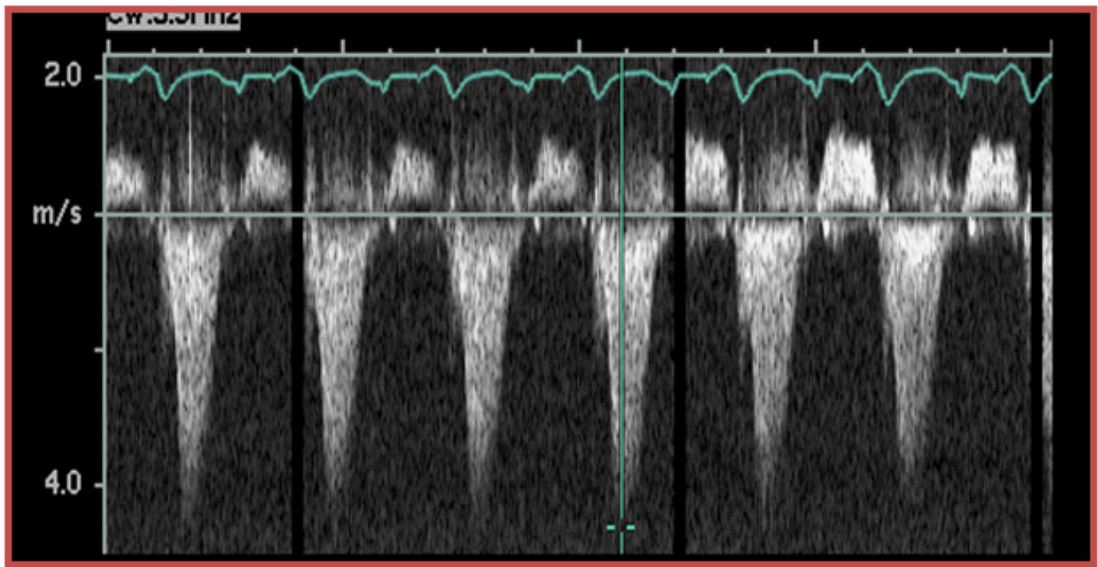


Figure 1: Continuous wave Doppler across the left ventricular outflow tract during systole. Again, gated to the cardiac cycle. The waveform indicates an approximately 4.0 m/sec velocity gradient.

In pulsed wave ultrasound, similar concepts apply however the electrical signal is generated in regular intervals. For example, 10 cycles will be produced with a pause interval of 20 cycles [3]. This is utilized similarly and a Doppler shift signal is analyzed to produce corresponding images. In pulse-wave Doppler systems, a single transducer and receiver are utilized (Figure 2). The pulse repetition frequency (PRF) determines the maximum velocity the instrument can detect and at high Doppler shifts reconstruction can be incorrect and the direction of flow will be reversed [4]. The Nyquist limit (Equation 2) states that ambiguity is avoided if Doppler shift is less than half the sampling frequency:

$$\text{Equation 2: } f_d < \frac{f_s}{2}$$

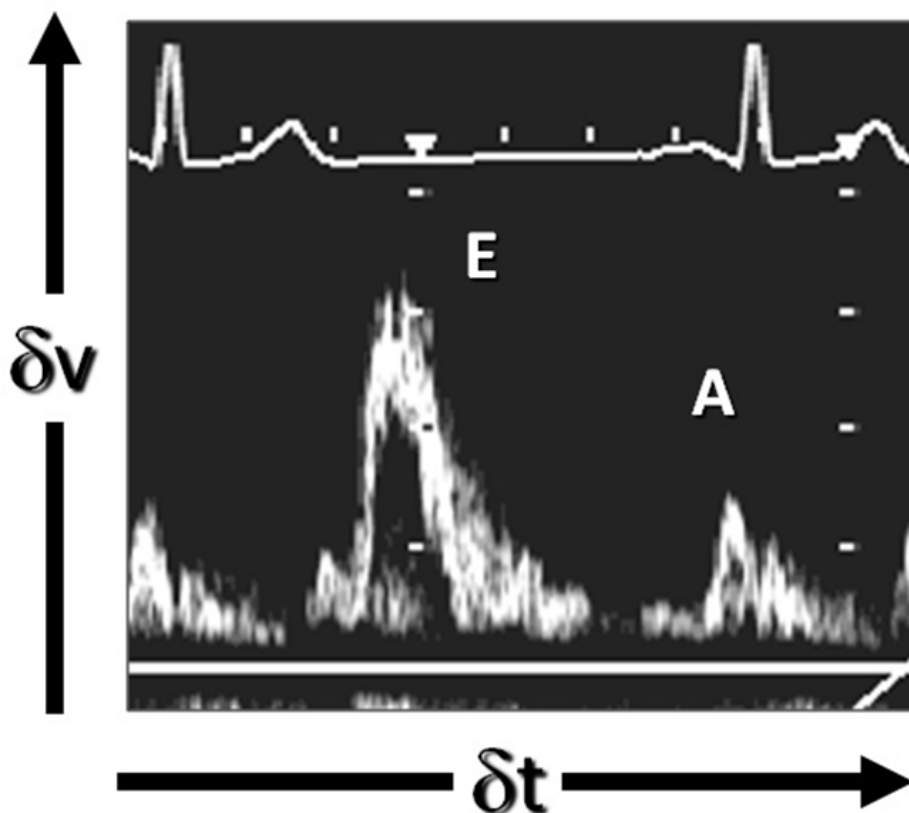


Figure 2: Pulsed wave Doppler of inflow across the mitral valve gated to the electrocardiogram (ECG). The characteristic early diastolic wave (E) from passive filling is followed by the active filling (A) from atrial contraction. The limitation of this modality is that it provides only the change in velocity (y-axis) over the change in time (x-axis).

This state of ambiguity is known as the aliasing artifact [2]. The classic example of aliasing comes from western films. As a stagecoach gets underway, its spokes are visualized rotating in the correct direction but as the rate of rotation approaches the frequency of the camera frame rate, they appear to reverse rotational direction [2,4]. This is the same process that occurs during pulse wave Doppler (Figure 3). It can be corrected by increasing the PRF, however this can cause an overlap in echoes produced by deep structures and if the echoes are strong enough, this can become superimposed on the more superficial object of interest. Therefore, in pulse wave Doppler, the PRF is maximized without causing overlap between echo trains. The maximum velocity (V_m) that can be accurately measured can be determined by:

$$\text{Equation 3: } V_m = \frac{c^2}{8 * R * f_t}$$

Where R is the range or distance from the transducer [3].

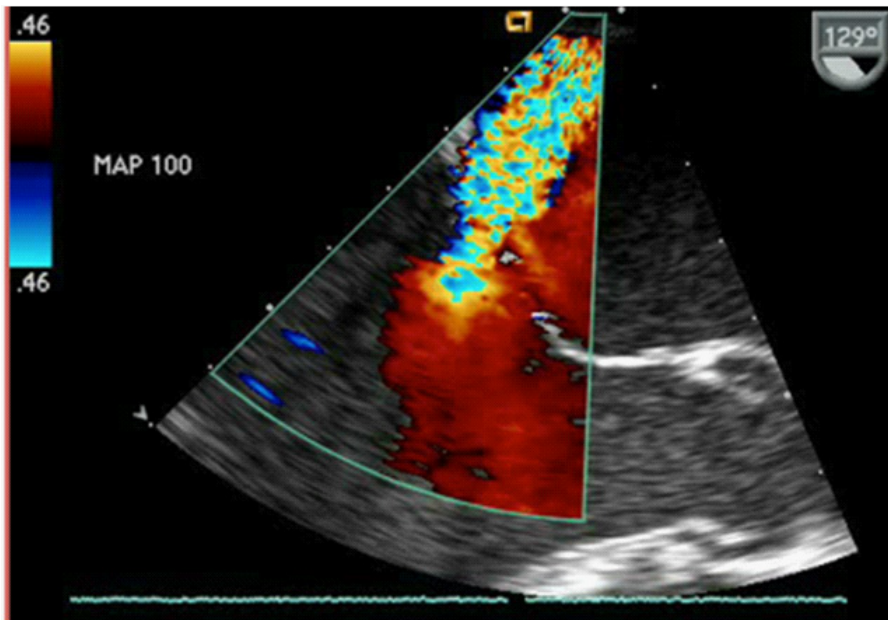


Figure 3: Color Doppler showing severe regurgitation from a leaking mitral valve. The high velocities from the turbulent regurgitant flow exceed the Nyquist limits of the settings that result in the characteristic ‘speckled’ colors. Adjusting the Nyquist settings on the ultrasound machine might provide a great range of velocities (upper and lower) but with a lower velocity resolution.

To increase measurable velocities, high pulse repetition frequency was developed. This method utilizes pulse wave Doppler at two to five different ultrasound bursts, increasing the sampling frequency and allowing for higher velocity measurements. Another alternative is continuous wave Doppler. This is not affected by the aliasing phenomena and is therefore used in high velocity situations such as when stenotic valves are evaluated.

Two other commonly used modalities include color Doppler imaging and power Doppler imaging. Each modality has its advantages and limitations. Color Doppler imaging is often used to determine flow rates and direction of flow. This delivers a depiction of mean Doppler shift that can be translated for mean velocity estimations. This modality is heavily dependent on the angle of the beam in relation to the vessel [3,5]. Power Doppler, is influenced little by the angle involved. It provides less information regarding the velocity or flow in a blood vessel but depicts a clearer anatomic picture due to its ability to reduce background noise. It is therefore often utilized to identify vasculature of interest prior to analysis with other methods [2].

In echocardiography, ultrasound has allowed for both 2-dimensional and 3-dimensional qualitative analysis of the cardiac system. The information obtained by Doppler, when interpreted with the application of fluid dynamics, allows for calculations of pressure gradients and flow velocities within the cardiac system. These fluid dynamic principles can be applied appropriately

only when there is a thorough understanding of hematologic properties and the assumptions utilized. When assumptions are incorrectly applied, inaccurate results adversely affect clinical decisions [6]. Other Doppler-derived variables are not based on fluid dynamics and were developed by direct observation. Regression formulas were developed to correlate the observations to variables of interest. This has inherent limitations and are only applicable to the specific anatomic and physiologic circumstances investigated in the studies. The use of Doppler-derived pressure half-time for mitral stenosis [7] and deceleration time for left ventricular operating stiffness are two such examples [8]. Nevertheless, despite limitations, Doppler echocardiography is a cornerstone tool for the assessment of cardiovascular structure and function.

HEMATOLOGIC PROPERTIES AND PRINCIPLES IN FLUID DYNAMICS

In all dynamic systems, flow characterization is complex and dependent upon the properties of the transported fluid. In the human body, blood is a variable suspension of particles within a viscous, compressible, non-Newtonian fluid that flows through compliant tubes that participates in both laminar and non-laminar flow. Its dynamics are affected by wave propagation, local hemodynamics, vessel expansion, and temporal wall shear stress gradients [9]. Without definition of properties and assumptions, this would be an impossible system to model.

In each model, a “black box” of interest is defined to allow mathematical analysis of blood in varying circumstances. A set of assumptions permits mathematical simplification of the situation. For example, in medium-to-large arteries, blood can be treated as a Newtonian fluid in laminar flow. This allows for application of the Navier-Stokes equation. The same assumptions cannot be applied to small arteries or capillaries, as the diameter of the vessels is similar to the size of the cells. Small vessels are therefore subject to increased wall interactions and turbulence caused by pulsatile flow [10].

Despite its compressible nature, blood can be treated as an incompressible fluid with a constant density allowing for simplified calculations and modeling. This is possible because the density of blood changes minutely in the time and volume intervals typically analyzed. Also, the effects of thermal expansion or contraction of volume are mitigated because of the narrow range of body temperature. With a constant density and defined volume, flow and pressure can be calculated under the principle of mass conservation. This assumption is a cornerstone for most models and has significant application when modeling flow within a ventricle and across valves.

Despite its shear-thinning properties, the assumption of constant viscosity is often applied. Viscosity gradients are greatest when shear forces are high such as at wall interfaces. The viscosity gradients within the heart are minimal as the majority of flow does not interact with wall surfaces and can therefore be negated and a constant viscosity. This combined with constant volume allows for the calculation of cross-sectional area or effective orifice area (EOA) [11]. These are a few examples how fluid dynamics can be clinically useful.

NAVIER-STOKES IN ECHOCARDIOGRAPHY

As mentioned, a primary application of the pulsed Doppler waveforms is the estimation of pressure gradients across valves, both native and prosthetic [12]. The basis of this is the Navier-Stokes equation for incompressible fluid. This is utilized to describe three-dimensional flow within the heart. The Navier-Stokes equation can then be rewritten to describe two-dimensional flow across a streamline – this is known as Euler’s equation (Equation 4) and relates the instantaneous local pressure (p) and velocity (v) as a function of distance (s) and time (t) [13].

Equation 4:
$$\frac{\partial p}{\partial s} = -\rho \left[\frac{\partial v}{\partial t} + v \frac{\partial v}{\partial s} \right]$$

Integrating the Euler equation between 2 points along a pathway (such as within the heart between a point in the left atrium and ventricle) results in the unsteady Bernoulli equation (Equation 5).

Equation 5:
$$\Delta p_c = \frac{1}{2} \rho (v_2^2[t] - v_1^2) + \rho \int_{s_{LA}}^{s_{LV}} \frac{\partial v[s,t]}{\partial t} ds + G$$

Similarly, the unsteady Bernoulli equation can be written as (Equation 6):

Equation 6:
$$\Delta p(t) = \frac{1}{2} \rho \Delta (v_2^2 - v_1^2) + M \frac{dv}{dt} + R(v) + G$$

The complete form of the unsteady Bernoulli equation can be broken down into 4 terms:

1. A **convective term** [$\Delta p_{conv} = \frac{1}{2} \rho \Delta (v_2^2 - v_1^2)$] accounts for the fall in pressure and the simultaneous rise in the kinetic energy as fluid increases velocity across an orifice.
2. An **inertial term** [$\Delta p_{INT} = M \frac{dv}{dt}$] describes the pressure change required to accelerate a mass of blood across the valve.
3. A **viscous term** [$\Delta p_{visc} = R(v)$] describes the loss of energy from the viscous interactions between the fluid along the walls.
4. A **gravitational term** [G] describes the effects of gravitational forces on the mass.

Where $\Delta p(t)$ is the drop in pressure as a function of time, ρ is blood density (1.05 g/cm³), v is the velocity of blood between the two points of interest (v_1 and v_2), and M is the inertance term of blood flow. R is a resistive term reflecting the effects of viscosity along the path, generally considered negligible and hence ignored. The reason for the assumption of the negligible contribution of resistive or viscous forces is based upon Poiseuille equation (Equation 7):

Equation 7:
$$\Delta p_{visc} = \frac{4\mu V_{max} L}{r^2}$$

The viscous resistance to flow (Δp_{visc}) is a function of the viscosity of blood (μ), the peak velocity (V_{max}), the length of the column (L), divided by the radius squared (r^2). For cardiac applications, steady-state laminar flow has been assumed. While this is known to not be the case within the heart and across valves, when applied within the range of human cardiac output (2-6 liters/minute), over the distance measured (typically only several centimeters within the heart),

and for the range of valvular or tubular diameters (also typically only several centimeters), the contribution of the resistance term ranges from 0.006 mmHg (for a diameter of 1.4 cm and a cardiac output of 2 liters/min) to 0.14 mmHg (for a diameter of 1.0 cm and a cardiac output of 6 liters/min) and is hence negligible [14]. Similarly, the gravitational effects are also considered negligible and are typically ignored [15].

Cardiac applications often describe blood flow originating in either the right or left atrium. The initial velocities within the left and right atriums are often negligible when assessing trans-tricuspid and trans-mitral flow [16]. However, this assumption does not always apply such as in cases of valvular regurgitation in which blood velocities are variable and retrograde flow can occur [17].

INTERTANCE FORCE

The intertance term, M , can be described as (Equation 8):

Equation 8:
$$M \approx \frac{(\Delta P_{act} - \Delta P_{conv})}{\left(\frac{dv}{dt}\right)}$$

In which M can be approximated as the difference between the actual pressure gradient (ΔP_{act}) and the convective component of the pressure gradient ($\Delta P_{conv} = \frac{1}{2}\rho\Delta[v^2]$) as a function of the changes in velocity over time.

For routine applications, M is typically negated because it requires deriving the change in velocity per unit time (acceleration) over a distance. This spatial acceleration is not available by conventional 2D Doppler velocity data, which only provides the velocity at a point of interest. For routine clinical applications, the estimation of a pressure gradient within the heart only considers the easy to measure convective term and assumes minimal contribution from inertance. However, this assumption was proven invalid [18]. While sophisticated analysis of color M-mode imaging has demonstrated the ability to determine the spatial acceleration of blood and the inertial component, these tools are not readily available for routine clinical applications. They can provide useful information for research applications (Figure 4a,b) and may someday be part of routine clinical evaluations [18].

It is application of all these assumptions that is commonly referred to as the “modified” Bernoulli equation (Equation 9):

Equation 9:
$$\Delta p = 4v^2$$

In which v is the Doppler derived velocity in m/sec and Δp is the estimated pressure gradient in mmHg. Again, an additional assumption is that the initial velocities, for example in the left atrium, are minimal and hence, only the final velocity is considered.

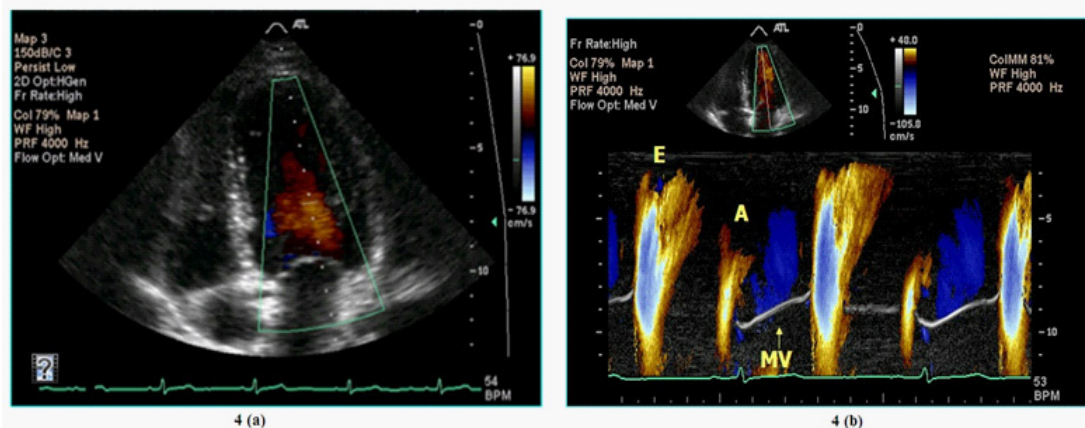


Figure 4: Two-dimensional color flow imaging of the left atrium and ventricle with the scan line oriented in alignment across the mitral valve (4a). The resulting color M-mode Doppler of flow across the mitral valve (MV), shows the characteristic early filling E-wave (E) and late A-wave (A). The images are acquired with ECG gating. Such images provide temporal (x-axis) and spatial (y-axis) flow into the left ventricle. The color bar (upper, middle right) can then be used to translate the colored pixels into corresponding velocities at a specific instant in time and space. The spatio-temporal velocity characteristics can then be used to solve for Euler's equation (see text) and determine an instantaneous pressure gradient between 2 points. A key limitation is that some echocardiographic machines use a non-linear color bar relationship (i.e. color code : velocity relationship) hence complicating clinical or research applications.

For nonrestrictive orifices, such as a normal valves and “larger” conduits these assumptions are not applicable. Because of the relatively large amount of blood that must pass through a non-restrictive valve with each cardiac cycle, the inertial term plays a significant role in describing the overall pressure gradient [19]. Although investigators demonstrated the importance of the inertial component of the Bernoulli equation when applied to transmitral flow, little work has been done to apply it clinically. It is often ignored despite its potentially significant contribution to an overall pressure gradient [11,20]. Previous human, animal, computer numerical modeling data suggests that the inertial components can be as great as 90% of the total pressure contribution (>12 mmHg) across the non-stenotic mitral valve [21] and may lead to a systemic underestimation during routine cardiac assessment [20].

VORTEX FLOW

The advent of vortex measurements and clinical application represents one facet of an increasingly exciting field in echocardiography. When a fluid is ejected from a positive displacement pump it creates a jet flow, if this flow is rapidly accelerating it will create a leading portion which rolls into a toroidal fluid mass which is referred to as a vortex ring [22]. This vortex produces larger mass and momentum transport phenomena than an equivalent straight jet of fluid which

has led to increasing interest in its biologic optimization for efficient fluid transport. This energy efficiency platform allows for merging of multiple streams without significant energy loss.

Vortex formation can be anticipated when Reynolds number (Re) (Equation 10) is greater than 6:

$$\text{Equation 10: } Re = \frac{vD}{\mu}$$

Where v is the velocity of fluid exiting the chamber, D is the diameter of the jet at the chamber exit (i.e. effective orifice diameter) and μ is the viscosity of the fluid. Vortex strength can be expressed as a function of velocity, in 2 dimensions this can be quantified as (Equation 11):

$$\text{Equation 11: } \omega(r, t) = \nabla * v = \left(\frac{\partial v_y}{\partial x} - \frac{\partial v_x}{\partial y} \right)$$

Where ω refers to the vorticity. When the curl operator is applied to the Navier-Stokes equation, vorticity of incompressible flow is defined as (Equation 12):

$$\text{Equation 12: } \partial_t \omega + (v \times \Delta) \omega = (\omega * \nabla) v + \rho \nabla^2 \omega$$

Where $(v * \Delta) \omega$ describes the convective transport of vorticity, $(\omega * \nabla) v$ represents the effect of velocity variation on vorticity, and $\rho \nabla^2 \omega$ the effect of viscosity. The vortex circulation (Γ) can be expressed as a function of angular velocity ($\vec{v}$) around a loop ($\vec{l}$) (Equation 13):

$$\text{Equation 13: } \Gamma(t) = \oint \vec{v} d\vec{l}$$

Vorticity develops preferentially in a shear layer adjacent to the tissue as a result of velocity differences between the flowing fluid and the solid boundary. This affects the pressure distribution within the chamber as well as the shear stresses particularly at the boundary layer (i.e. chamber wall).

The formation of vortices and its potential for clinical implications have been studied for a number of years [23]. The analysis of vortex formation in the human heart has been applied to multiple imaging modalities including MRI and echocardiography. A number of studies have compared vortex formation in healthy subjects with those with a variety of cardiac dysfunctions such as atrial fibrillation and dilated cardiomyopathy. These have shown that in healthy subjects vortex formation is characterized as compact, dynamic, pulsatile and elliptical that occurs simultaneously without collision within the heart chambers [24]. These vortices are maintained in both diastole and systole. The disruption of these vortices may contribute to the formation of thrombus and the decrease in cardiac efficiency in diseased states [25].

In the healthy heart, the direction of flow through the mitral outflow is towards the posterolateral wall of the ventricle. This generates a vortex within the left ventricle that directs flow towards the aortic outflow track with minimal loss of energy. This redirection is believed to increase the efficiency of the system. If this system is disrupted, such as in hypertrophied or dilated states, this vortex would be inefficient and thus increased intraventricular pressure (muscle contraction) would be necessary for the same outflow volume and velocity. This would lead to increased endothelial wall stress with disruption of the geometry of the left ventricle.

With increased understanding of the importance of vorticity to the human heart an increase in imaging modality has occurred. Recently, particle imaging velocimetry (PIV) techniques have been incorporated as well as Doppler evaluation [25]. An increasing effort has been made to study healthy human subjects in order to define normal vortex formation. This will allow identification of clinically relevant irregularities in diseased states. The integration of PIV to echocardiography has led to new items of interest including total dissipation, kinetic energy fluctuation, the square vorticity fluctuation, and the turbulent shear stress [19]. Other suggested parameters include vortex formation time and eccentricity index, and untwisting rate [26,27]. No single variable has emerged as a clinically relevant indicator at this time.

Vortex formation and propagation of fluid flow is intimately linked with the wringing motion of the heart. Current understanding supports the progression of LV filling which begins as the LV pressure declines just before mitral valve opening, the LV wall recoils slightly from the elastic nature of the tissues, causing a pressure gradient which accelerates the filling of the ventricle [25,26]. This effect is referred to as the left ventricle suction effect [28]. Diastolic intraventricular pressure gradients are proposed to be linked to systolic function and provide a mechanism by which the ventricle can fill in the setting of low pressures; in healthy ventricles it is an active process, in diseases ventricles (with diastolic dysfunction) a passive process [29]. As the elastic wall springs outward towards a neutral state, the valve opens; fluid flow in the direction of the posterolateral ventricle wall causes the formation of two vortex rings. As fluid fills the chamber, a gradual deceleration is apparent at the apex that causes a pressure gradient directed from the apex to the base of the ventricle. This change in pressure distribution aids in acceleration of the fluid around the vortex with redirection towards to the aortic orifice [25]. The smooth transition and utilization of the inherent elastic nature of the ventricle walls creates a remarkably efficient flow generation that is dependent on appropriate pressure distributions.

Even with this ever-growing body of knowledge, our ability to identify clinically relevant criteria is dependent on reliable, consistent imaging. Echocardiography is already the most utilized cardiac imaging modality and this is sure to be an area of expanded clinical application.

CONCLUSION

It is well known that the heart is a dynamic system that not only contracts in the longitudinal axis but also rotates around a long-axis causing a wringing (twisting) motion. The mathematical equations that define these relationships in two and three dimensions can be simplified in quantitative assessments of cardiovascular structure and function. However, while these simplified equations can be used to estimate pressure, temporal flow, and velocity relationships, an understanding of the fundamentals of fluid dynamics and the inherent limitations of their simplification is critical to proper application. This is obvious to the observer during open-heart surgeries but is much harder to quantify and observe in the noninvasive setting. Echocardiography has been at the forefront of qualitative and quantitative cardiac function

testing since its' development. With a thorough understanding of fluid dynamics the clinically relevant interpretation of ultrasound technology continues to expand. An increasing emphasis on pressure and flow characterization within the heart highlights this need for continued fluid dynamic analysis. With our growing body of information and an ever-expanding understanding of cardiac mechanics, the role of echocardiography will continue to expand.

GLOSSARY

B-Mode: A mode of ultrasound imaging in which the brightness of the corresponding image dots is directly related to the amplitude of the ultrasound signal.

Boundary Layer: layer of fluid immediately adjacent to a surface; flow is significantly affected by viscosity and shear forces

c : speed of the ultrasound wave

D : Diameter of effective orifice

EOA: effective orifice area

f_D : Doppler shift

f_r : returning frequency

f_t : transmitted frequency

Incompressible fluid: fluid in which the density does not vary with flow velocity, thus the viscosity is also constant

L : length of the column

Laminar Flow: smooth flow of fluid without turbulence, eddies, or cross currents; predicted flow pattern of $Re < 2300$

Non-Laminar Flow: occurs at $Re > 4000$; characterized by eddies, vortices, cross currents, turbulence; dominated by inertial forces

LV: left ventricle

M : inertance term of blood flow (see text)

Newtonian Fluid: fluid with viscous stresses linearly proportional to strain rate (i.e. rate of change of deformation over time)

Non-Newtonian Fluid: any fluid in which the viscosity, shear stress, and strain rate are linearly proportional (i.e. shear thickening or shear thinning fluids); example—ketchup, blood

PIV: particle imaging velocimetry

PRF: Pulse repetition frequency

Re: Reynolds number; ratio of viscous forces to momentum forces which yields a dimensionless number utilized to predict flow patterns

R: range or distance from the transducer

r: radius

$u \cos \theta$: velocity component of the reflection in the direction of the ultrasonic beam

V_m : Maximum velocity which can be accurately measured in pulse wave Doppler

$V_{\max}$: peak velocity

v : Doppler derived velocity

θ : angle between the line of movement of the reflector and the transducer beam

ρ : Density of blood, 1.05 g/cm³

μ : the viscosity of blood

v : velocity of blood

ω : vorticity

Δp : estimated pressure gradient

Δp_{visc} : viscous resistance to flow

Γ : vortex circulation

$\vec{v}$: angular velocity

$\vec{l}$: loop of vortex trajectory

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