31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

Determination of early diastolic LV vortex formation time (T*) via the PDF formalism: a kinematic model of filling

Erina Ghosh, Leonid Shmuylovich and Sándor J. Kovács *Member, IEEE*

***Abstract*- The filling (diastolic) function of the human left ventricle is most commonly assessed by echocardiography, a non-invasive imaging modality. To quantify diastolic function (DF) empiric indices are obtained from the features (height, duration, area) of transmitral flow velocity contour, obtained by echocardiography. The parameterized diastolic filling (PDF) formalism is a kinematic model developed by Kovács et al which incorporates the suction pump attribute of the left ventricle and facilitates DF quantitation by analysis of echocardiographic transmitral flow velocity contours in terms of stiffness (k), relaxation (c) and load (x_o). A complementary approach developed by Gharib et al, uses fluid mechanics and characterizes DF in terms of vortex formation time (T^*) derived from streamline features formed by the jet of blood aspirated into the ventricle. Both of these methods characterize DF using a causality-based approach. In this paper, we derive T^*'s kinematic analogue $T^*_{kinematic}$ in terms of k, c and x_o. A comparison between $T^*_{kinematic}$ and $T^*_{fluid\ mechanic}$ obtained from averaged transmitral velocity and mitral annulus diameter, is presented. We found that T^* calculated by the two methods were comparable and $T^*_{kinematic}$ correlated with the peak LV recoil driving force kx_o.**

I. Introduction

The prevalence of heart failure has reached 'epidemic' proportions [1, 8] and about 50% of heart failure admissions have heart failure with a normal ejection fraction (HFNEF) or diastolic heart failure [2,4]. The prognosis for HFNEF vs. HF with low ejection fraction is essentially indistinguishable [4, 11] and HFNEF patients constitute a heterogeneous group, hence the ability to elucidate and characterize the stiffness and relaxation components of diastolic dysfunction (DD) is important.

However, noninvasive imaging based diagnosis of DD has been primarily empiric and correlation based rather than causal mechanism based. Attempts to quantify DF using echocardiography have generally focused on selected aspects of blood or tissue motion, of chamber size, shape or volume.

Manuscript received on April 7, 2009. This work was supported in part by the National Institutes of Health, the Whitaker Foundation (Roslyn, VA), the Alan A. and Edith L. Wolff Charitable Trust (St Louis, MO), the American Heart Association and the Barnes-Jewish Hospital Foundation.

E.G is with the department of Biomedical Engineering, School of Engineering and Applied Sciences, Washington University in St. Louis- 63130 (email: eghosh@wustl.edu).

L.S is with the department of Physics, College of Arts and Sciences, Washington University in St. Louis - 63130 ( ).

S.J.K is with the Cardiovascular Division, Department of Internal Medicine, Washington University in St. Louis- 63110 (email: sjk@wuphys.wustl.edu).

In order to quantify DF and provide insight into the mechanisms, LV filling has been modeled using kinematic [8], fluid mechanics [5, 6], and electrical circuit analogs [9]. The fundamental physiologic and causal governing principle of DF is that the LV initiates filling by serving as a mechanical suction pump. The potential energy to power the recoil process is stored elastic strain. The release of this strain is modulated by spatiotemporal chamber wall relaxation. Because the energy source for diastolic recoil (wall-motion) resides in tissue, blood is passive and behaves in accordance with the laws of fluid mechanics and the pressure gradients generated by wall-motion. Since both blood and tissue are incompressible, their motions are necessarily closely coupled, particularly since the four-chambered heart is, to within about 95%, a constant-volume pump [12].

Previous work [6] considered vortex formation by blood as it enters the LV through the mitral valve during the early, suction initiated, rapid filling, including its optimized redirection to facilitate ejection in the subsequent systole. It has been demonstrated that filling via vortex formation is more efficient than a straight jet of blood. Vortex formation in early diastole has been characterized in terms of the vortex formation time T^* [10] a dimensionless parameter defined by the ratio of the effective aspirated jet or plug-flow length to the effective plug-flow diameter. Importantly, thrust generated by the vortex is maximized when the vortex reaches its maximum circulation. Vortex formation time independently correlated with trans-mitral thrust, minimal ventricular pressure and pressure drop time-constant. Thus T^* can serve as a dimensionless, fluid-mechanics derived, global index of DF [5].

Since at mitral valve opening, and for a brief interval thereafter, LV pressure drops while LV volume increases (dP/dV<0), all human hearts initiate filling as mechanical suction pumps. Accordingly, suction initiated filling and ventricular DF can be modeled kinematically via the parameterized diastolic filling (PDF) formalism. This formalism characterizes filling in analogy to the kinematics of a simple harmonic oscillator (SHO). The velocity of transmitral flow (Doppler E-wave) is predicted in accordance with the laws of SHO motion. It is parametrized by spring constant-k, damping constant-c and SHO initial displacement-x_o. By using the clinical Doppler E-wave contour as input, one can solve the 'inverse problem' of diastole and compute the three, unique, independent parameters x_o, c and k for each E-wave. Thus these parameters, and indexes computed from them can quantitate LV DF in kinematic terms [8].

We hypothesized that kinematic and fluid mechanics based characterization of DF are equivalent. Therefore we derived $T^*_{kinematic}$ in terms of the PDF parameters and determined its correlation with $T^*_{fluid\ mechanic}$, [6]. This method defines T^* as ratio of time averaged transmitral flow velocity over the duration of the early filling to the maximum mitral valve annulus area.

II. Method

Theory: T from Fluid mechanics*

The definition of vortex formation time (T^*) is

$$T^* = \int_0^t \frac{U(t)}{D(t)} \cdot dt \qquad (1)$$

where $U(t)$ is transmitral blood flow velocity, t is the duration of E-wave and $D(t)$ is mitral annulus diameter. Gharib et al [6] calculate the vortex formation time as

$$T^*_{fluidmechanic} = \frac{\overline{U}}{\overline{D}} \cdot t \qquad (2)$$

where $\overline{U}$ is the mean transmitral blood flow velocity, t is the duration of E-wave and $\overline{D}$ is the mitral annulus diameter. Transmitral flow was measured via trans-thoracic echocardiography via pulsed Doppler. The annulus diameter was obtained from long-axis apical views of the heart at the peak flow from M-mode images.

Theory: Kinematic modeling

T^* can also be expressed in terms of the transmitral blood flow velocity (E-wave) and mitral annulus velocity (E'-wave). The equations that provide the contour each of these waves utilize the PDF parameters – k, c and x_o for the E-wave and k', c' and x_o' for the E'-wave. The left ventricle at the onset of the E-wave is approximated as a right circular cylinder with external radius R, internal radius r_1 and height l_1. The ventricle expands during filling to internal radius r_2 and height l_2. In accordance with the constant volume feature the external radius remains the same. The volume of blood entering the ventricle is

$$\frac{\pi}{4}(D(t))^2 \cdot E(t) \cdot t = \pi r_2^2 l_2 - \pi r_1^2 l_1 \qquad (3)$$

where t is the duration of the E-wave and $E(t)$ represents the transmitral blood flow velocity (same as $U(t)$). Assuming that the volume of ventricular tissue is conserved during filling

$$\pi(R^2 - r_1^2) l_1 = \pi(R^2 - r_2^2) l_2$$

$$\Rightarrow \pi(r_2^2 l_2 - r_1^2 l_1) = \pi R^2 (l_2 - l_1) \qquad (4)$$

Substituting (4) in the expression for volume of blood flowing into the ventricle (3) and solving for $D(t)$ we get,

$$R^2(l_2 - l_1) = (D(t))^2 \cdot E(t) \cdot t \cdot \frac{1}{4}$$

$$\Rightarrow 4 \cdot R^2 \cdot E'(t) = (D(t))^2 \cdot E(t)$$

$$\Rightarrow \frac{1}{D(t)} = \frac{1}{2R} \cdot \sqrt{\frac{E(t)}{E'(t)}} \qquad (5)$$

where E'(t) is the mitral annulus velocity. Substituting $D(t)$ into (1) gives,

$$T^* = \frac{1}{2R} \int_0^t E(t) \cdot \sqrt{\frac{E(t)}{E'(t)}} \cdot dt$$

$$\Rightarrow T^* = \frac{1}{2R} \int_0^t \sqrt{\frac{(E(t))^3}{(E'(t))}} \cdot dt \qquad (6)$$

The PDF formalism provides, closed form algebraic expressions for E-wave and E'-wave contours which are solutions to the SHO equation of motion. For underdamped kinematics (c^2-$4mk<0$) the E-wave and E'-wave are:

$$E(t) = -\frac{kx_o}{m\omega} e^{\frac{-ct}{2}} (\sin(\omega t))$$

$$E'(t) = -\frac{k' x_o'}{m\omega'} e^{\frac{-c't}{2}} (\sin(\omega' t))$$

For over-damped kinematics the expressions are

$$E(t) = -\frac{kx_o}{m\omega} e^{\frac{-ct}{2}} (\sinh \omega t)$$

$$E'(t) = -\frac{k' x_o'}{m\omega'} e^{\frac{-c't}{2}} (\sinh \omega' t)$$

Where $\omega = \sqrt{(4mk - c^2)}/2m$ $\omega' = \sqrt{(4mk' - c'^2)}/2m$ for under-damped kinematics and $\omega = \sqrt{(c^2 - 4mk)}/2m$ $\omega' = \sqrt{(c'^2 - 4mk')}/2m$ for over-damped kinematics.

Substituting into (6) yields the vortex formation time in terms of PDF parameters. For the underdamped regime:

$$T^*_{kinematic} = K \int_0^t \sqrt{\frac{\sin^3(\omega t)}{\sin(\omega' t)}} e^{\frac{-t(3c - c')}{4}} dt \qquad (7)$$

For overdamped regime:

$$T^*_{kinematic} = K \int_0^t \sqrt{\frac{\sinh^3(\omega t)}{\sinh^3(\omega' t)}} e^{\frac{-t(3c - c')}{4}} dt \qquad (8)$$

Where $K = \frac{1}{2R} \cdot \sqrt{\frac{k^3 x_o^3 \omega'}{k' x_o' \omega^3}}$

Theory: T from PDF parameters*

A numerical simulation using Matlab (Matlab 6.0, MathWorks, Natick, MA) was done to calculate $T^*_{kinematic}$ from the PDF parameters. The E-wave parameters x_o, c and k, the E'-wave parameters – x_o', c and k' were generated using a random number generator assuming a uniform distribution. The limits of the distribution for each parameter were determined using values obtained by fitting actual E- and E'-waves with the PDF model. The six parameters were used to calculate the $T^*_{kinematic}$ using (7) and (8) and integrating over the duration of the E'-wave. The $T^*_{kinematic}$ value was taken as the value of vortex formation time at the time the E'-wave velocity maximum (E'$_{peak}$).

Comparison of $T^*_{kinematic}$ with $T^*_{fluid\ mechanic}$

$T^*_{fluid\ mechanic}$ was calculated using the mean E-wave velocity and the mitral annulus diameter at peak diastole. The vortex formation time was calculated for the whole duration of the E-wave. To compare the $T^*_{kinematic}$ obtained from the PDF model to the $T^*_{fluid\ mechanic}$ derived in [6], we calculated $T^*_{fluid\ mechanic}$ using Eq. 2 and averaging the E- wave velocity over time. The mitral annulus area was taken to be 4 cm^2 [7]. Since $T^*_{kinematic}$ was calculated at instant of peak E'-wave velocity we extrapolated it to the end of E-wave.

III. Results

The simulation program generated E- and E'-waves and calculated the vortex formation time as function of time. The vortex formation time was plotted against time and $T^*_{kinematic}$ was determined. The extrapolated value of $T^*_{kinematic}$ was determined. The vortex formation time ($T^*_{fluid\ mechanic}$) was determined using the method in [6]. The two vortex formation times were compared. The results are shown below.

A sample E- and E'-wave generated by the simulation and the $T^*_{kinematic}$ plotted against time is shown in Fig. 1. The selected E- and E'-waves are underdamped. The peak velocity of E-wave is 32 cm/s and peak velocity of E'-wave is 8 cm/s. The $T^*_{kinematic}$ has been plotted for the duration of E'-wave (0.174s). The time point of peak E'-wave velocity has been marked in the figure. The vortex formation time at this point is 3.4. The extrapolated value of $T^*_{kinematic}$ is 14.6. The $T^*_{fluid\ mechanic}$ calculated using the same E-and E'-wave is 2.4. In agreement with prior observation, the dimensionless vortex formation time increases linearly with time till near the end of E'-wave [5].

IV. Discussion

Historically, alternative approaches have been used to model LV filling and characterize the operative physiologic mechanisms. These include electrical circuit analog models, finite element fluid-tissue interaction models, lumped parameter fluid-chamber models and kinematic models. Most of these approaches involve coupled, nonlinear partial differential equations with up to dozens of parameters, all of which need to be specified at the initiation of model computation. These types of models are not 'invertible', i.e. model parameters cannot be uniquely determined from physiologic data used as input. Two of the approaches can use physiologic data as input to determine model predicted parameters. These include a kinematic approach, the PDF formalism, and the fluid mechanics approach advanced by Gharib [6].

In Gharib's fluid mechanics approach, diastolic function of the chamber is quantitated in terms of vortex formation time. Because the chamber is part of a constant volume 4-chamber pump, tissue motion is necessarily accompanied by fluid motion. Given the approximate shape of the LV as a truncated ellipsoid of revolution that recoils by long axis extension during diastole with concomitant radial expansion of the interior of the chamber wall, the geometry of the arrangement assures that the blood aspirated by the left ventricle in early diastole forms an asymmetric vortex ring [13].

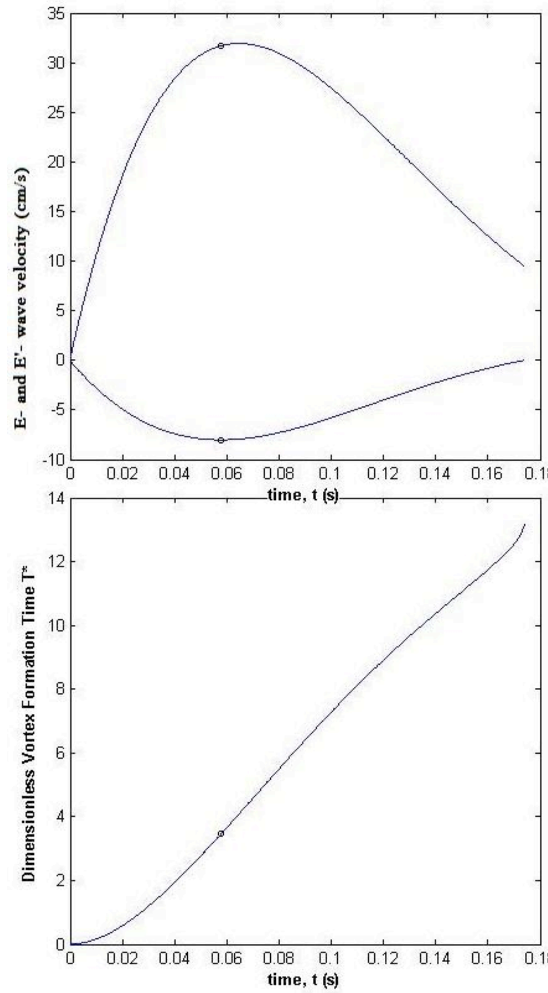

Fig 1. (Top) E-wave (positive velocity curve) and E'-wave (negative velocity curve) plotted against time. (Bottom) $T^*_{kinematic}$ plotted against time for the duration of E'-wave. The PDF parameters for this set of waves were: k= 300 3g/s^2, c= 23g/s, x_o = 3.9cm, k' = 434 g/s^2, c' = 21 1g/s, x_o'= 0.7cm

This arrangement has important biological and fluid mechanics advantages. The biological advantage is that vortex formation 'rinses' the endocardial surface with each heart beat, thereby avoiding areas of stagnation that can form thrombi and generate arterial obstruction outside the heart. The fluid mechanics advantage is that fluid transport into a closed container with an expanding inner boundary is made more efficient by development of a vortex ring. This is characterized by the vortex formation time, determined by time-averaged speed of transmitral flow (E-wave), the duration of the flow relative to the diameter of the orifice (mitral annulus diameter). Previous work [6, 10] has focused on finding an optimal value of the vortex formation time (T^*) which can be used as an index of diastolic function. Also T^* has been shown to independently correlate with the transmitral thrust, minimum LV pressure and the pressure drop time constant of isovolumic relaxation [5].

The left ventricle during early diastole acts as a suction pump and the elastance and recoil of the ventricular wall provides the energy for the pressure gradient which aspirates blood from the atrium into the ventricle. Hence we hypothesized that the vortex formation time could be calculated from modeling filing kinematically in terms of the analog stiffness, damping and initial spring displacement of an equivalent SHO. Consistent with known physiology, we assumed that the external radial dimension of the left ventricle remains constant during the filling so that the ventricle lengthens as its wall thins while it fills. Using the constant volume attribute of this simplified, and idealized geometric atrio-ventricular arrangement [12], time varying mitral valve diameter was calculated in terms of the epicardial dimension and the ratio of transmitral blood flow velocity (E-wave) and the mitral annulus velocity (E'-wave). This approach allowed for the determination of T^* without a direct measurement of time varying mitral diameter. Using the PDF formalism, we expressed the E- and the E'-wave contours in terms of SHO kinematics.

We derived the expression for T^* as a function of time in terms of PDF parameters. This expression provides T^* at every instant during the E-wave. By calculating the instantaneous values of transmitral blood velocity and the mitral annulus diameter this method also provides a value of the vortex formation time. For consistency with the constant volume atrioventricular chamber approximation we calculated the vortex formation time up to the duration of the E'-wave. We denoted the vortex formation time at the peak of E'-wave as $T^*_{kinematic}$. Previous work [5] has shown that T^* increases linearly with time. Hence we linearly extrapolated $T^*_{kinematic}$ to the end of the E-wave. We calculated the $T^*_{fluid\ mechanic}$ by taking the E-wave velocity averaged over the duration of E-wave, the maximum mitral annulus diameter and the duration of the E-wave.

We found that the $T^*_{kinematic}$ and $T^*_{fluid\ mechanic}$ were comparable and correlated well with each other (R^2= 0.44), consistent within the approximations of our geometric model indicating the applicability of our approach to calculate vortex formation time. In addition, we also found that $T^*_{kinematic}$ was strongly correlated ($R^2 = 0.517$) with peak driving force of transmitral flow (kx_o) and the rate of change of the transmitral flow velocity ($R^2 = 0.377$, E_{peak}/ E_{dur}).

Acknowledgements- Discussions with Wei Zhang are gratefully acknowledged.

REFERENCES

1. A.M Katz. "The Modern View of Heart Failure: How Did We Get Here?" *Circ Heart Fail.* . 2008; 1:63-71.
2. M.T. Maeder, D.M. Kaye. "Heart Failure With Normal Left Ventricular Ejection Fraction." *J. Am. Coll. Cardiol.* 2009;53;905-918.
3. G Hong, G Pedrizzetti, G Tonti, P Li, Z Wei, J.K. Kim, A Baweja, S Liu, N Chung, H Houle, J Narula, M.A. Vannan. "Characterization and Quantification of Vortex Flow in the Human Left Ventricle by Contrast Echocardiography Using Vector Particle Image Velocimetry." *J. Am. Coll. Cardiol. Img*. 2008;1;705-717.
4. V Melenovsky, B.A. Borlaug, B Rosen, I Hay, L Ferruci, C.H. Morell, E.G. Lakatta, S.S. Najjer, D.A. Kass. "Cardiovascular Features of Heart Failure With Preserved Ejection Fraction Versus Nonfailing Hypertensive Left Ventricular Hypertrophy in the Urban Baltimore Community The Role of Atrial Remodeling/Dysfunction." *J Am Coll Cardiol* 2007;49:198–207
5. A Kheradavar, M Gharib. "On Mitral Valve Dynamics and its Connection to Early Diastolic Flow." *Annals of Biomedical Engineering* 2009; 37:1-13.
6. M Gharib, E Rambod, A Kheradavar, D.J. Sahn, J.O. Dabiri. "Optimal vortex formation as an index of cardiac health." *Proc. Natl. Acad. Sci.* Vol. 103 pp. 6305-6308. April, 2006.
7. J Lisauskas, J Singh, M Curtois, S. J. Kovács. "The relation of the peak Doppler E-Wave to peak mitral annulus velocity ratio to diastolic function." *Ultrasound in Med. & Biol*. Vol. 27 pp. 499-507, 2001.
8. S. J. Kovács, B Barzilai, J.E. Pérez. "Evaluation of diastolic function with Doppler echocardiography: the PDF formalism." *Am J Physiol*. 87: H178-H187, 1987.
9. S. J. Kovács, J.S. Meisner, E.L. Yellin. "Modeling of diastole." In: *Cardiology Clinics*, edited by MH Crawford and S. J. Kovács. Philadelphia, PA: Saunders, 2000, p. 459-487.
10. A Kheradavar, M Milano, M Gharib. "Correlation between vortex ring formation and mitral annulus dynamics during ventricular rapid filling." *ASAIO J* 52(1): 34-38, 2006.
11. M. Gheorghidae, P.S. Pang. "Acute Heart Failure Syndromes." *J. Am. Coll. Cardiol*. 2009;53;557-573.
12. A.W. Bowman, S. J. Kovács. "Assessment and consequences of the constant-volume attribute of the four-chambered heart." Am J Physiol Heart Circ Physiol. 285(5): H 2027-33 Nov. 2003.
13. S.J. Kovács, D.M. McQueen, C.S. Peskin. "Modeling cardiac fluid dynamics and diastolic function." *Phil. Trans. R. Soc. Lond. A* 359: 1299-1314, 2001.